

WHERE THE HEART MEETS THE MIND'S EYE: ASSOCIATIONS BETWEEN
CARDIAC MEASURES OF AUTONOMIC ACTIVITY AND SELECTIVE
ATTENTION IN CHILDREN AND ADULTS

by

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DISSERTATION ABSTRACT

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Title: Where the Heart Meets the Mind's Eye: Associations Between Cardiac Measures of Autonomic Activity and Selective Attention in Children and Adults

Multiple theoretical frameworks posit that interactions between the autonomic nervous system and higher-order neural networks are crucial for cognitive regulation. However, few studies have directly examined whether autonomic physiology influences brain activity during cognitive tasks, and even fewer of those studies have examined both autonomic branches when doing so. Measures of selective attention derived from event-related brain potentials (ERPs) are particularly well-suited for addressing this question, given that ERP selective attention tasks are designed to control for the influences of psychomotor processes and arousal and are predictive of higher-order cognitive function in children and adults. Such research is particularly promising for understanding how early adversity impacts neurocognitive development in children, given that stress experienced early in life impacts both autonomic function and selective attention.

Here, a broad literature review is presented, integrating findings across studies of autonomic physiology, cognition, and brain activity in children and adults (Chapter 1). Then, two experiments are described where cardiac measures of parasympathetic and sympathetic activity were recorded concurrently with ERPs during an auditory selective task in a sample of adults (Chapter 2) and in a sample of preschool-aged children

(Chapter 3). Results from both experiments demonstrate a key role for the sympathetic nervous system in selective attention for adults and children, such that greater sympathetic activity is associated with larger effects of selective attention on ERPs. These findings are then reviewed with suggestions for how existing models of neurovisceral integration might be updated to better emphasize the role of sympathetic nervous system activity in neurocognitive processes, emphasizing measures of threat-related and reward-related arousal, as represented by galvanic skin response and pre-ejection period, respectively (Chapter 4). Future directions are also discussed, including recommendations for future studies of neurovisceral integration to examine associations between physiology, behavior, and brain activity at the single-trial level, to incorporate participants from more diverse backgrounds of life experience, and to examine the plasticity of autonomic mechanisms implicated in neurocognitive function.

This dissertation includes unpublished coauthored material.

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CHAPTER I

GENERAL INTRODUCTION

Psychophysiological studies of attention are historically represented by largely separate bodies of literature, with brain-based measures primarily employed in tightly-controlled manipulations of spatial and feature-based attention (e.g., Hillyard, Hink, Schwent, & Picton, 1973; Fukuda & Vogel, 2009), and peripheral measures of autonomic physiology utilized in attention paradigms emphasizing the regulation of physiology and affect (e.g. Hansen, Johnsen, & Thayer, 2003; Johnsen et al., 2003; Park, Vasey, Van Bavel, & Thayer, 2013). According to the model of neurovisceral integration, measures of brain and autonomic activity both contribute to attentional control, such that top-down control signals from the prefrontal cortex interact with the parasympathetic nervous system (PNS) to coordinate an optimal level of engagement with fluctuating task demands (Smith, Thayer, Khalsa, & Lane, 2017; Thayer & Lane, 2000; 2009). However, the neurovisceral integration model is primarily based on studies of autonomic physiology, in particular studies employing measures of the PNS such as high-frequency heart rate variability (HF-HRV), and as a result a majority of the model's claims concern the role of the PNS and do not describe how PNS activity interacts with specific measures of brain function. Further, a number of studies have demonstrated associations between activity of the sympathetic nervous system (SNS) and measures of brain and behavior during cognitive tasks (Beissner, Meissner, Bar, & Napadow, 2013; Hajcak, McDonald, & Simons, 2003; 2004). For example, we recently demonstrated that measures of the PNS and SNS interact to predict individual differences in WM performance (Giuliano, Gatzke-Kopp, Roos, & Skowron, in press). Thus, a primary aim

of the present studies was to clarify the joint contributions of the PNS and SNS to the neurovisceral model by directly examining associations between activity of both autonomic branches and neural activity underlying attentional control.

Unpacking the contributions of PNS and SNS activity to neurocognitive function is of great potential relevance to research seeking to explain the effects of chronic stress on neurocognitive function and brain development. Exposure to chronic stress has been associated with global changes in brain volume and function, along with specific deficits in higher-order cognitive processes such as working memory and selective attention (Hanson et al., 2010; 2012; 2013; Karlamangla et al., 2014; Stevens, Lauinger, & Neville, 2009). Many of the regions of the brain particularly impacted by chronic stress exposure are also regions shown to be associated with activity of the PNS and SNS, in particular the amygdala, hippocampus, and medial prefrontal cortex (Beissner et al., 2013; Smith et al., 2017). This raises the hypothesis that the effects of chronic stress exposure on neurocognitive outcomes are mediated by effects of chronic stress exposure on autonomic mechanisms that contribute to neurocognitive function. The neurovisceral model stipulates that the role of autonomic function in facilitating cognitive performance is to maintain an optimal level of arousal, accelerating heart rate when the context calls for increased processing demands in a flexible and dynamic manner (Thayer & Lane, 2009). Given that chronic stress exposure has been associated with profound alterations in arousal and autonomic function as early as the prenatal environment (Propper & Holochwest, 2013), it is possible that less flexible and/or context appropriate levels of autonomic arousal might be an important contributor to deficits in cognitive function seen in individuals who are experiencing chronic stress (Giuliano et al., in press).

This dissertation is a direct inquiry into the idea that autonomic activity is related to neurocognitive function underlying attentional control by measuring PNS and SNS function in the context of a selective attention task. The task employed is well suited to this inquiry because movement-related psychomotor confounds are controlled for, and event-related brain responses recorded during this task have been shown to predict performance on separate measures of cognitive function in adults and children (Giuliano, Karns, Neville, & Hillyard, 2014; Isbell, Wray, & Neville, 2015). In addition, this dissertation examines the role of chronic stress on autonomic and neurocognitive measures by assessing exposure to risk factors associated with socioeconomic status (SES) such as household income, parental education, and marital status. Where effects of risk exposure were associated with autonomic and neurocognitive measures, mediation models were tested to examine whether autonomic activity mediated the associations between risk exposure and neurocognitive measures.

Before moving on to the two experiments presented herein, a larger overview of the neurovisceral integration model is presented. This is followed by a discussion of findings not typically included in the neurovisceral framework and how these findings might be integrated into the model for a more holistic representation of the autonomic branches. Concluding the general introduction of this work, an overview of subsequent chapters is presented with a brief discussion of findings and theoretical relevance.

Neurovisceral Integration

The neurovisceral integration model is based on a rich body of pharmacological and anatomical studies demonstrating connections between neural activity and the regulation of autonomic function, with particular regard to autonomic effects on cardiac

function (Thayer & Lane, 2000; 2009). A key feature of this model, and related models such as Porges' polyvagal theory (2001; 2007), is an emphasis on the role of the vagus nerve, the Xth cranial nerve, which bidirectionally enervates the brainstem and heart and serves to enact control of cardiac function by the parasympathetic nervous system (PNS). In many species including humans, cortical activity has been shown to impact heart rate, such that activation of the vagus leads to slowing of interbeat intervals within milliseconds (Levy, 1990). Thus, activity of the vagus, and the PNS by proxy, is typically approximated by measuring heart rate variability in high-frequency bandwidths (HF-HRV) or respiratory sinus arrhythmia (RSA), which quantify changes in heart rate occurring at such short time scales.

Neurovisceral integration theory largely focuses on a body of studies demonstrating that greater vagal activity, as measured by higher levels of HF-HRV, is associated with better performance on a variety of cognitive measures, better affective regulation, and differences in resting blood flow and activity in various cortical regions (Smith, Thayer, Khalsa, & Lane, 2017; Thayer, Ahs, Fredrikson, Sollers, & Wager, 2012). Given that the vagus inhibits heart rate, and that measures of the vagus are associated with better inhibition of affect and behavior, as well as blood flow in areas of the brain involved in top-down regulation, Thayer and Lane (2000; 2009) argue that HF-HRV or "cardiac vagal tone" is a general index of activity in inhibitory circuits of the brain. These circuits have been proposed to include the ventromedial prefrontal cortex, anterior cingulate cortex, and amygdala (Thayer et al., 2012), however it should be noted this was not supported by a large-scale study of cerebral blood flow, cognition, and HF-HRV in 490 older adults (Jennings, Allen, Gianaros, Thayer, & Manuck, 2015). Most

recently, proponents of the neurovisceral integration model detailed a richly integrated hierarchy of eight levels of biological and function systems underlying interactions between peripheral physiology and brain function (Smith, Thayer, Khalsa, & Lane, 2017). While this model addresses the role of diverse modulatory signals in the hierarchy of top-down control, including peripheral cardiovascular reflexes and noradrenergic systems that serve as core components of the SNS, the primary conclusions of the model concern HF-HRV as an index of integration across neural and physiological systems.

It is interesting to ponder whether the neurovisceral model has had some success at least in part due to the appeal of the idea of a single biological indicator of ‘body’ demonstrating strong associations with a unitary function of ‘mind’. In fact, the phrase “mind-body” and appeals to mind-body practices can be found in multiple papers presenting the neurovisceral integration model (Smith, Thayer, Khalsa, & Lane, 2017; Thayer & Lane, 2000). Similarly, it is appealing to summarize a function of the vagus nerve as somewhat of an executive system that is primarily responsible for cross-talk between ‘body’ and ‘mind’ with emotional and social regulation being facilitated by turning on the vagus (Porges, 2001; 2007). While physiological studies have clearly demonstrated a central role for the vagus in autonomic activity and interactions between autonomic and central nervous systems (Levy, 1990), this does not exclude the possibility that other pathways exist by which autonomic activity influences cortical activity, and vice-versa. Given that evidence does exist for associations of cortical activity and cognitive function with measures that are not vagally-mediated, in particular measures of the sympathetic nervous system (SNS)(Beissner, Meissner, Bar, & Napadow, 2013), it is

important to consider how these findings could be integrated with the neurovisceral framework.

Theoretical Gaps to be Addressed

Traditionally, the neurovisceral model has acknowledged that activity of the sympathetic autonomic branch is involved in the cortical regulation of heart rate but focuses on the role of HF-HRV as an index of top-down regulation, with sympathetic influences conceptualized as more bottom-up (Smith et al., 2017; Thayer & Lane, 2009). As a result, a majority of experimental work within the neurovisceral framework exclusively measures HF-HRV in association with cognition (Park, Vasey, Van Bavel, & Thayer, 2013; Williams, Thayer, & Koenig, 2016).

This sole focus on HF-HRV is problematic for a number of reasons. First, this methodology does not account for bottom-up sympathetic influences, shown to interact with top-down parasympathetic function in regulating heart rate (Berntson, Cacioppo, & Quigley, 1993a) and have independent effects on arousal and orienting responses (Hugdahl, 1996). Second, to date there has not been an exhaustive examination of associations between higher-order neurocognitive function and SNS activity, so it is premature to exclude measures of SNS activity from studies of neurovisceral integration, which may be due to implicit assumption that SNS measures will not provide added information above and beyond that conveyed by PNS measures of HF-HRV. This is particularly true given that a number of studies have identified associations between SNS activity, cognitive function, and activity in higher-order regions of the brain such as the prefrontal cortex (Beissner, Meissner, Bar, & Napadow, 2013). Finally and more broadly, there has not been an exhaustive examination of the contributions of both autonomic

branches to neuroimaging measures in humans. The most recent meta-analysis of neuroimaging studies including autonomic measures found only 11 studies employing measures of cognitive function, and none of these studies included measures of both the PNS and SNS (Beissner et al., 2013). Simply put, more research is needed to support the claim that HF-HRV has an exclusive role in scaffolding neurocognitive function.

Another challenge in understanding links between SNS and brain function is that a majority of studies have quantified SNS activity via galvanic skin response (Beissner et al., 2013; Hajcak, McDonald, & Simons, 2003; 2004; Hugdahl, 1996). Galvanic skin response is an index of the electrodermal system, an aspect of the SNS that is classically more involved in threat-related processing (Dawson, Schell, & Filion, 2007). In contrast, other studies have started measuring SNS activity via pre-ejection period (PEP), which indexes the SNS-mediated ejection of blood through the left ventricle during the heart cycle, and is believed to represent reward-related processes of the SNS (Brenner & Beauchaine, 2011). Consistent with this distinction between threat- and reward-related SNS activity, PEP, but not galvanic skin response, has been shown to shorten in anticipation of rewards and predict later reward-seeking behavior (Derefinko et al., 2016). Moreover, a number of studies have implicated PEP in behavioral regulation, such that reduced PEP reactivity to incentives may be a risk factor for the development of externalizing behaviors and ADHD in children and adolescents (Beauchaine, Gatzke-Kopp, & Mead, 2007; Crowell et al., 2006). Similar results have been observed in association with longer resting PEP, such that children with less trait-like reward-related SNS activity are rated higher on dimensions of problem behaviors and aggression (Beauchaine et al., 2013). What remains to be seen is the extent to which reward-related

SNS activity is associated with neurocognitive function, and how SNS activity may interact with PNS activity and potential associations between PNS activity and neurocognitive function.

By including both measures of SNS and PNS, a larger goal of this dissertation is to attempt to integrate the neurovisceral framework with the notion of autonomic space, which states that autonomic function should be conceptualized as interactions between parasympathetic and sympathetic space (Berntson, Cacioppo, & Quigley, 1993b; Berntson, Cacioppo, & Fieldstone, 1996). Experimental support for this idea has shown that the efficiency of PNS activation for regulating heart rate depends on concurrent activation of the SNS (Levy, 1990). Reciprocal PNS and SNS activity, such as PNS increases concurrent with SNS decreases and SNS increases concurrent with PNS decreases, is often an adaptive biological response (Berntson, Cacioppo, & Quigley, 1993b). For example, El-Sheikh and colleagues (2009) have reported that reciprocal PNS and SNS activity may represent a healthy sign of coordinated development amongst biological systems in children exposed to higher degrees of early life stress. Similarly, in adults, we recently showed that a pattern of reciprocal PNS-dominance was associated with better working memory performance in adults, such that better working memory scores were seen in individuals with lower resting SNS activity and greater PNS reactivity (Giuliano, Gatzke-Kopp, Roos, & Skowron, in press). By applying the autonomic space framework to the neurovisceral model, the classically observed findings between PNS and cognition can be extended to include details about what contexts, and for whom, interactions with SNS activity become particularly relevant.

Overview of Experiments

The research conducted here utilized the same event-related potential (ERP) measure of selective attention in adults and preschool-aged children in order to examine associations between selective-attention ERPs and measures of PNS and SNS activity, as indexed by HF-HRV and PEP. Effects of selective attention were quantified as the relative difference in the brain response to sounds that were to-be-attended relative to sounds that were to-be-ignored. Participants were recruited as part of a broader study of dual-generation approaches to parenting training in which adults and children were recruited as a family unit. Families were recruited due to their affiliation with Head Start services, therefore all participants were living in homes near or below the U.S. federal poverty line. To account for this, risk exposure was quantified with a cumulative assessment of household income, family marital status, and maternal education.

In the first experiment on ninety-three adults (Chapter II), basic associations were observed between ERP selective attention effects and resting levels of HF-HRV and PEP. Higher resting HF-HRV and shorter resting PEP were associated with larger modulation of selective attention at the N1 ERP component. Regression models including all variables of interest suggested that resting HF-HRV and PEP made unique contributions to the N1 attention effect, with no evidence of interactions between the two resting measures. No associations with current risk exposure were observed, but this is not particularly surprising given that risk exposure early in life has been more proximally related to brain and autonomic function than exposure later in life. These findings generally support the neurovisceral integration model by demonstrating associations between higher HF-HRV and more optimal neurocognitive function, and extend this model to demonstrate a similar role for SNS activity as measured by PEP. Consistent

with views of PEP as a reward-related index of the SNS, the association between shorter PEP and larger effects of selective attention raise the possibility that reward-related arousal is an important individual difference to consider when evaluating cognitive function.

In the second experiment of 103 preschool-aged children (Chapter III), resting PEP values were similarly associated with ERPs during the selective attention task, but no associations with HF-HRV were observed. At the group level, we replicated a previously observed relationship between SES and attention, such that children exposed to more SES-related risk factors showed an enhancement of their ERP to distractor sounds with increasing risk exposure. Critically, the relationship between higher risk exposure and larger ERPs to distractor sounds was fully mediated by PEP values. These results highlight the importance of measuring the SNS when examining neurovisceral integration in younger populations, and suggest that such measures may underlie disruptions in higher-order cognitive function commonly observed with increasing exposure to adversity (e.g., Hanson et al., 2012; 2013).

This dissertation contains previously co-authored material. The study described in Chapter III has been submitted for peer-review in *Developmental Psychology* and was co-authored with C.M. Karns, L.E. Roos, T.A. Bell, S. Petersen, E.A. Skowron, H.J. Neville, & E. Pakulak.

CHAPTER II

PARASYMPATHETIC AND SYMPATHETIC CONTRIBUTIONS TO INDIVIDUAL DIFFERENCES IN NEURAL MECHANISMS OF SELECTIVE ATTENTION IN ADULTS

This work is in preparation for submission to the *Journal of Experimental Psychology: General*, therefore the following chapter is formatted according to the journal's publication standard, American Psychological Association format.

Introduction

A number of researchers have postulated a critical role for the peripheral nervous system in activity of the central nervous system. Models of neurovisceral integration (Thayer & Lane, 2000; 2009) and polyvagal theory (Porges, 2001) describe similar theoretical frameworks wherein autonomic activity, in particular activity of the parasympathetic nervous system (PNS), is critical for higher-order behavior and cognition due to the high-degree of interconnectedness between neural and peripheral structures regulating behavior and physiological state (Smith, Thayer, Khalsa, & Lane, 2017). However, surprisingly few studies have directly tested associations between autonomic measures and brain activity (Beissner, Meissner, Bar, & Napadow, 2013). Among studies that have examined links between cognitive performance and autonomic physiology, most have focused singularly on measures indexing the PNS (e.g., Thayer & Lane, 2009; Park & Thayer, 2014) or sympathetic nervous system (SNS) activity (e.g., Hajcak, McDonald, & Simons, 2003). Few studies have characterized the joint impact of

PNS and SNS measures on cognition or underlying neural processes. This is particularly relevant given a wealth of evidence from animal and human studies that autonomic regulation does not operate on a continuum from PNS to SNS dominance, but instead should be conceptualized as interactions between activity in each branch of ‘autonomic space’ (Berntson, Cacioppo, Quigley, 1993b; Berntson, Cacioppo, Quigley, & Fabro, 1994). Supporting this framework, we recently found that interactions between PNS and SNS function were associated with individual differences in performance on a difficult working memory task (Giuliano, Gatzke-Kopp, Roos, & Skowron, *in press*). Here, we aimed to extend these findings by examining the association between PNS and SNS function and neural mechanisms of selective attention, using a variant of a classic event-related potential (ERP) task designed to control for physiological arousal and minimize psychomotor confounds (Hillyard, Hink, Schwent, & Picton, 1973).

Selective attention offers an ideal cognitive mechanism for the examination of interactions between neural mechanisms and autonomic physiology. First, and primarily, neural mechanisms of selective attention can easily be studied in the absence of manual responses, and further, within contexts where participants are asked to sit calmly and relaxed (e.g., Giuliano, Karns, Neville, & Hillyard, 2014). Motor responses have been shown to be a confound for the interpretation of PNS and SNS measures (Bush, Aikon, Obradovic, Stamperdahl, & Boyce, 2011), yet a majority of the literature demonstrating a relationship between cognitive function and autonomic physiology is based on performance on tasks that require manual, speeded responses (Hansen, Johnsen, & Thayer, 2003; Hansen, Johnsen, Sollers, Stenvik, & Thayer, 2004; Johnsen et al., 2003; Park, Vasey, van Bavel, & Thayer, 2013; Saus et al., 2006; Williams, Thayer, & Koenig,

2016). Second, ERP studies of selective attention studies have been designed to further control for arousal by measuring effects of selective attention at the relative difference in the brain response to simultaneously presented to-be-attended and to-be-unattended stimuli (Hillyard, Hink, Schwent, & Picton, 1973). However, it is unclear whether individual differences in physiological measures of arousal influence the pattern of selective attention effects classically observed in this ERP paradigm. We are not aware of any ERP study of selective attention that has tested PNS and SNS contributions to effects of selective attention. Third, selective attention is a core cognitive skill implicated in a variety of higher-order processes (Cowan et al., 2005; Garon, Bryson, & Smith, 2008; Fukuda, Vogel, Mayr, & Awh, 2010), and the ERP measure of selective attention used here has been shown to predict higher-order cognitive function in children and adults (Giuliano, Karns, Neville, & Hillyard, 2014; Isbell, Wray, & Neville, 2015), therefore any observed relationship between neural mechanisms of selective attention and autonomic physiology would potentially be relevant for a large body of related cognitive mechanisms. Finally, the ERP selective attention task used here possesses a high degree of ecological validity and applicability to a wide variety of research samples. Task demands involve sitting still and listening to a narrator within a crowded auditory environment, much like one might be asked to do within an academic or professional context, or even when enjoying leisure time activities. A number of studies have demonstrated that this task is suitable for measuring selective attention from three years of age to adulthood (Karns, Isbell, Giuliano, & Neville, 2015; Sanders, Stevens, Coch, & Neville, 2006), including samples at-risk for chronic stress exposure and low socioeconomic status (Neville et al., 2013; Stevens, Lauinger, & Neville, 2009).

Parasympathetic nervous system and cognition

A majority of the literature on associations between autonomic physiology and cognitive performance is centered on findings that higher resting activity of the PNS often serves as a trait-like marker of regulatory capacity across contexts (Beauchaine & Thayer, 2015; Holzman & Bridgett, 2017). PNS activity is typically quantified as high-frequency heart rate variability (HF-HRV) or respiratory sinus arrhythmia (RSA), both of which are measures of the amount of variability in heart rate that occurs in the respiration bandwidth (Berntson, Cacioppo, & Quigley, 1993a). Activation of the PNS is associated with greater power in the high frequency bandwidth, and serves to quickly decelerate heart rate via projections of the vagal nerve between the brain stem and heart. According to neurovisceral integration theory (Thayer & Lane, 2000; 2009), higher resting levels of HF-HRV or RSA and the associated higher degree of variability in PNS activation reflects a greater capacity for flexible engagement to changes in environmental demands, and is often referred to as an individual's "vagal tone" (for a commentary, see Berntson, Cacioppo, & Grossman, 2007).

A growing body of evidence suggests that the association between PNS activity and self-regulation extends to domains of cognitive control. For example, on laboratory measures of cognitive ability, adults with higher resting HF-HRV have been shown to have faster and less variable reaction times during target detection tasks (Williams, Thayer, & Koenig, 2016), reaction times that are less affected by the presence of distractors (Park, Vasey, Van Bavel, & Thayer, 2013), faster reaction times during the Eriksen flanker task (Alderman & Olson, 2014), more accurate performance on measures of working memory and sustained attention (Hansen, Johnsen, & Thayer, 2003), and

more accurate performance on Stroop tasks in the presence of an additional cognitive load (Capuana, Dywan, Tays, Elmers, Witherspoon, & Segalowitz, 2014). However, this general finding of a positive association between resting HF-HRV activity and performance on laboratory tasks has a relatively small effect size, with evidence of publication bias towards small significant effects, suggesting this relationship should be interpreted with caution (Zahn, et al., 2016). One explanation for why small effect sizes are observed may be that resting PNS activity is not associated with cognition broadly, but rather is specifically associated with so-called ‘executive’ processes that emphasize attentional control and inhibition (Kimhy et al., 2013; Spangler, Bell, Deater-Deckard, 2015).

PNS activity has often been reported to decline or ‘withdrawal’ in response to a cognitive challenge (Melis & van Boxtel, 2001; 2007), with an increasing degree of HF-HRV withdrawal reported with increasing task difficulty (Backs & Seljos, 1994; Byrd, Reuther, McNamara, DeLucca, & Berg, 2014; Lenneman & Backs, 2009). There is some evidence that greater HF-HRV withdrawal is associated with faster response times on the Stroop task (Mathewson et al., 2010). However, the directionality of the relationship between PNS reactivity and cognition appears to be context dependent, as increases in HF-HRV activity relative to baseline have been reported in response to challenges that require more regulation of affect (Butler, Wilhelm, & Gross, 2006; Park, Vasey, Van Bavel, & Thayer, 2014; Segerstrom & Nes, 2007).

Sympathetic nervous system and cognition

In contrast to the importance of resting measures of the PNS for behavior, contributions of the SNS to behavior are typically conceptualized in terms of reactivity. A

number of studies have demonstrated that cognitive challenges tend to elicit increases in SNS activation (Allen & Crowell, 1989; Backs & Seljos, 1995; Berntson et al., 1994; Berntson, Cacioppo, & Fieldstone, 1996). However, research by Melis and van Boxtel (2001; 2007) suggests that SNS reactivity is more often seen in association with poor cognitive performance, while PNS reactivity is more relevant to behavior amongst good performers. In separate studies measuring HF-HRV and skin conductance levels during a variety of cognitive tasks, an overall reactivity pattern of HF-HRV withdrawal and increase in skin conductance to the tasks was observed, consistent with previous research. Results from both studies showed that, when comparing good and poor performers, good performers showed a larger effect of PNS withdrawal to the task and had performance that was primarily predicted by PNS withdrawal, while the performance of poor performers was more strongly associated with SNS activation (Melis & van Boxtel, 2001; 2007). These results are supported by findings from separate studies showing that PNS but not SNS measures are associated with reaction times during a modified Stroop task (Johnsen et al., 2003) and Eriksen flanker task (Alderman & Olson, 2014).

It is important to note that many studies of the SNS have relied on measures of galvanic skin response or skin conductance levels, which have been shown to reflect more peripheral fight-or-flight arousal of the electrodermal system (Dawson et al., 2007). Increasingly, studies are employing measures of cardiac pre-ejection period (PEP), a central measure of SNS influences on heart rate derived from the difference in time between the onset of a heart beat (Q point of the QRS complex) and the ejection of blood into the left ventricle, such that greater SNS activation drives shorter ejection intervals (Lozano et al., 2007). PEP has been shown to be more related to reward-sensitive

dimensions of the SNS, which include mesolimbic dopaminergic networks also implicated in cardiac regulation (Beauchaine, 2001; Brenner & Beauchaine, 2011). Dissociations between the influence of electrodermal activity and PEP on behavior suggest that electrodermal activity indexes the behavioral inhibition system and avoidance behaviors, while PEP indexes the behavioral activation system and reward-seeking behaviors (Derefinko et al., 2016; Hinnant, Erath, Tu, & El-Sheikh, 2016). Given that reward-sensitivity of mesolimbic dopaminergic processes has been implicated in individual differences in cognition as demonstrated by measures of pupillometry (Tsukahara, Harrison, & Engle, 2016), it follows that reward-related aspects of the SNS indexed by PEP might be more generally associated with cognition than the avoidance-related aspects of the SNS indexed by electrodermal measures.

Studies linking neural and autonomic measures

Although a number of meta-analyses have implicated brain function in autonomic activity, there is not a clear consensus on how underlying cortical structures give rise to the regulation of PNS and SNS measures. Based on a review of eight studies, Thayer and colleagues (2012) identified the amygdala and ventromedial prefrontal cortex (PFC) as critical regions implicated in PNS regulation (Thayer, Ahs, Fredrikson, Sollers, & Wager, 2012). Within the neurovisceral framework, the authors argue that HF-HRV reflects the degree to which top-down signals emanating from the medial PFC are integrated with brainstem structures regulating cardiac arousal. A separate meta-analysis of 43 neuroimaging studies employing autonomic measures identified significant contributions of both the PNS and SNS to brain activity (Beissner, Meissner, Bar, & Napadow, 2013). Within a subset of eleven studies that measured physiology during cognitive tasks, SNS

activity as measured by skin conductance levels was associated with activity in the ventromedial PFC, subgenual anterior cingulate cortex, and amygdala; conversely, PNS activity as measured by HF-HRV was only associated with activity in the anterior insula and amygdala. A separate study of resting brain perfusion similarly found that resting HF-HRV was associated with greater resting blood flow in the anterior insula and amygdala but not in prefrontal regions (Allen, Jennings, Gianaros, Thayer, & Manuck, 2015). Interestingly, a recent theoretical paper emphasizing the role of the PNS for neurovisceral integration does not cite the work by Beissner and colleagues (Smither, Thayer, Khalsa, & Lane, 2017), suggesting that the neurovisceral model should be updated to include evidence documenting the influence of the SNS on activity in midline prefrontal regions.

Few studies have examined associations between electrophysiological measures of brain activity and measures of autonomic activity. Among the few studies employing ERPs and autonomic measures, Hajcak and colleagues have found that ERPs time-locked to response errors are associated with SNS measures of skin conductance (Hajcak, McDonald, & Simons, 2003; 2004). Other studies have examined associations between power in different bandwidths of the electroencephalogram (EEG) and autonomic activity. Greater theta power (4-7 Hz) over frontal midline electrodes during an attention-demanding task, an index of attentional control, has been associated with increasing SNS and PNS influences on heart rate (Kubota et al., 2001). At higher bandwidths, asymmetry in alpha power (8-12 Hz) has been associated with SNS measures of skin conductance but not PNS measures of HF-HRV (Gatzke-Kopp, Jetha, & Segalowitz, 2014). Similarly, low-frequency beta power (13-20 Hz) has been reported to decrease in power with

increasing SNS activity, as measured by low-frequency HRV, but was not associated with HF-HRV (Triggiani et al., 2015). As the above review of findings demonstrates, both the SNS and PNS are implicated in measures of brain activity, yet there is still relatively little evidence for associations between autonomic and brain activity with regard to individual differences in performance.

The current study

Here we aimed to characterize PNS and SNS function during a selective attention task and clarify how PNS and SNS activity relates to concurrent neural measures of selective attention. HF-HRV and PEP were measured as indices of PNS and SNS function, respectively, during a 5-minute neutral film clip and subsequently during four separate stories of an auditory attention task designed for the recording of ERPs.

Analyses focused on modulations of selective attention on the ERP elicited by sound probes presented at to-be-attended and to-be-ignored spatial locations, and associations between modulations of selective attention on ERPs with measures of HF-HRV and PEP at baseline and during the task. Based on previous research, we hypothesized that higher baseline HF-HRV would be associated with larger ERP effects of selective attention. Additionally, we hypothesized that greater SNS arousal, as indexed by shorter PEP, would be associated with larger ERP effects of selective attention.

Method

Participants

Adults were recruited along with their children as part of a broader study testing a two-generation training program integrated into Head Start services. Adults were eligible to participate in laboratory visits if they were English language dominant, had no history

of neurological impairment, and normal or corrected-to-normal vision.

Electroencephalogram (EEG) measures were successfully obtained from 129 adults.

Seven adults declined placement of electrodes for measurement of electrocardiogram (ECG), eighteen adults did not have appropriately event-marked ECG data, and eleven adults had unusable impedance cardiogram (IC) data at baseline ($n = 4$), during the task ($n = 4$), or both ($n = 3$). This left 93 adults with complete data (87 females; age, $M = 32.56$ years, $SD = 7.51$, range = 32 to 67 years). Given that the sample was predominantly female, all analyses were duplicated without the six male participants and are reported in the supplementary results (see Supplemental Tables 1 and 2).

Adult participants enrolled in this study were all parents of a child currently enrolled in Head Start, and thus by definition all adults were from families living at or below the poverty line. To quantify the degree of exposure to risk factors related to low socioeconomic status, we calculated a cumulative index based on three discrete, additive markers: household income, maternal education, and maternal marital status (Evans & Kim, 2013). For each of the three indicators, risk was coded dichotomously as present (1) or not present (0), with each risk factor aimed to characterize the riskiest third of the sample for that dimension. Household income risk was quantified as households in the bottom third of annual incomes within the sample, here annual incomes less than \$40,000 ($N=37$). Maternal education risk was quantified as households in which the mother's highest degree of education was a high school diploma or less ($N=30$). Marital status risk was quantified as single parent households, in this case all single-mothers ($N=30$). As noted in the results below, analyses examining associations between cumulative SES

risks and the individual risk factors separately showed no associations with ERPs elicited during the selective attention task or any of the measures of autonomic physiology.

Measures

Auditory selective attention task. We used the same auditory attention ERP paradigm as our previous studies with child and adult participants (Karns, Isbell, Giuliano, & Neville, 2015; Neville et al., 2013; Stevens et al., 2009; Sanders et al., 2006; Coch et al., 2005). Participants were cued to selectively attend to one of two simultaneously presented children's stories differing in location (left/right loudspeaker), narrator's voice (a male or female reading the entire story aloud), and content. Illustrations from the story being read from the attended loudspeaker were presented on a monitor. A green arrow pointing to the left or right was displayed on the monitor throughout each block to indicate the side of the to-be-attended narrative.

ERPs were recorded to 100 ms duration probe stimuli embedded in both to-be-attended and to-be-unattended narratives. Probe stimuli were either linguistic (a voiced syllable) or nonlinguistic (a broad-spectrum buzz). The linguistic probe was the syllable /ba/, spoken by a female (a different voice from all the story narrators). The nonlinguistic probe was created by scrambling 4-6ms segments of the /ba/ stimulus, which preserved many of the acoustic properties of the linguistic probe. Across the stories, approximately 200 linguistic and 200 nonlinguistic probes were presented in each channel. The probes were presented randomly at an inter-stimulus interval (ISI) of either 200, 500, or 1000ms in one of the two loudspeakers at a time, with a range of plus or minus 25 ms of jitter for each ISI. The stories were presented at an average of 60 dB SPL, and the intensity of the probes was 70 dB. A researcher monitored adults throughout the task to ensure that they

remained still and equidistant between the two loudspeakers, and to administer comprehension questions via intercom following each pair of simultaneously presented stories.

Within each testing session, a total of eight different stories were presented. Since two stories were presented simultaneously, there were a total of four listening blocks. The stories were selected from the following children's book series: *Blue Kangaroo* (Clark, 1998, 2000, 2002, 2003), *Harry the Dog* (Zion & Graham, 1956, 1960, 1965, 1976), *Max & Ruby* (Wells, 1997, 2000, 2002, 2004), and *Munsch for Kids* (Munsch & Martchenko, 1989, 2001, 2002; Munsch & Suomalainen, 1995). In each of the four blocks, two stories were presented simultaneously with attention directed to the story played from either the left or right loudspeaker and read aloud by a different narrator from four narrators in total. For example, in one block, a participant could be directed to listen to the left loudspeaker, which might play a story read by a female narrator, while ignoring the right loudspeaker, which would be playing a story read by a male narrator; the illustrations on the monitor would correspond to the attended story. Each participant attended twice to a story on the right side and twice to a story on the left side, with start side counterbalanced across participants. For each participant, an individual narrator would be heard once as the narrator for an attended story and once as the narrator for an unattended story. After each story, an experimenter asked the participant three open-ended comprehension questions about the attended story to reinforce the goal of paying attention. The comprehension questions were written to emphasize multiple pieces of information that occurred throughout the entire course of the story. Verbal responses were coded by the

experimenter, who marked any keywords of the true answer spoken by the participant when answering the question.

Electroencephalogram (EEG). During the dichotic listening task, EEG was recorded at a sampling rate of 512 Hz from 64 Ag/Ag-Cl-tipped scalp electrodes (BioSemi Active2, Amsterdam, Netherlands) arranged according to the international 10–20 system. Electrode offsets were maintained at ± 30 μ V or less throughout each recording session. Additional electrodes were placed on the outer canthus of each eye, below the right eye, and on the left and right mastoids. The EEG was recorded relative to the common mode sense active electrode and then re-referenced offline to the algebraic mean of the left and right mastoids. Horizontal eye movements were plotted as the difference between the left and right outer canthus channels. Vertical eye movement, including eye blinks, were plotted as the difference between the lower right eye electrode and Fp1 (right anterior-most electrode). ERP analyses were carried out using EEGLAB (Delorme & Makeig, 2004) and ERPLAB (Lopez-Calderon & Luck, 2014). Raw EEG data were imported into EEGLAB and high-pass filtered at 0.1 Hz. Then, epochs time-locked to sound probes embedded in the dichotic listening task were extracted from -100 to 500 msec relative to probe onset. Epochs containing large voltage deviations or muscle/movement artifacts were identified by visual inspection and excluded from further analysis. Remaining data were then submitted to artifact rejection procedures within ERPLAB. Artifacts were identified based on moving window peak-to-peak changes in eye channels across a 200 ms window, moving in 50 ms increments. Individual artifact rejection parameters were adjusted for each subject to identify the smallest amplitude changes associated with eye movements or blinks. Manual artifact

rejection was employed after the automatic ERPLAB procedures, to ensure accuracy of artifact marking. Following artifact rejection, epochs were low-pass filtered at 40 Hz.

In order to facilitate analyses of the distribution of ERP effects and to reduce the number of multiple comparisons across electrode sites, we averaged the 64 electrodes into nine electrode clusters representing the scalp with distributional factors in a 3x3 design of anteriority (anterior, central, posterior) x laterality (left, medial, and right). The electrode clusters consisted of Left Anterior (AF3, AF7, F3, F5, F7), Medial Anterior (AFz, Fz, F1, F2), Right Anterior (AF4, AF8, F4, F6, F8), Left Central (FC3, FC5, C3, C5, FT7, T7), Medial Central (FCz, Cz, FC1, FC2, C1, C2), Right Central (FC4, FC6, C4, C6, FT8, T8), Left Posterior (CP3, CP5, P3, P5, P7, PO3, PO7, TP7), Medial Posterior (CPz, Pz, POz, CP1, CP2, P1, P2), and Right Posterior (CP4, CP6, P4, P6, P8, PO4, PO8, TP8). Mean amplitudes were extracted from time-windows of interest and subjected to an attention (2) x anteriority (3) x laterality (3) repeated-measures ANOVA to examine effects of selective attention. At time windows where there were significant effects of attention on ERP amplitudes, we examined associations between ERPs, HF-HRV, and PEP. In order to reduce the number of multiple comparisons, we averaged across electrode clusters demonstrating significant effects of attention, then examined partial correlations between ERP amplitudes and baseline HF-HRV, HF-HRV reactivity, baseline PEP, and PEP reactivity. Significant associations were followed with an examination of partial correlations with attended and unattended ERPs separately. Then, linear regression models were run to examine significant relationships between ERP effects of attention and physiological measures when including all four physiological measures in the model, with stepwise entering of age, then baseline HF-HRV and

baseline PEP, followed by HF-HRV reactivity and PEP reactivity. After these primary ERP analyses, we then explored correlations between ERPs and HF-HRV and PEP across the scalp, including correlations with SES risk levels.¹.

Cardiovascular physiology. A montage of 11 electrodes was used for the measurement of high-frequency heart rate variability (HF-HRV) and pre-ejection period (PEP). Electrocardiogram (ECG) was obtained from three disposable pre-gelled electrodes placed in a modified Lead II configuration on the distal right clavicle, lower left rib, and lower right abdomen. Impedance cardiogram (ICG; Z0) was recorded from eight electrodes placed in a tetrapolar configuration on the left and right lateral neck and torso, from a vertical maximum of the jawline down to the diaphragm. Data were acquired wirelessly via Biopac Nomadix BN-RSPEC and BN-NICO transmitters (Biopac Systems Inc, Goleta, CA) sending ECG and impedance signals respectively to a Biopac MP-150 acquisition unit placed in the room with the participant. A respiration signal was derived from the raw impedance cardiogram for the inspection of respiration values. High-frequency HF-HRV values were derived from natural log-transformed values of the spectral power in the high frequency range commonly used for adults (.12-.40 Hz). PEP was calculated from the first-order derivative of the cardiovascular impedance signal (dZ/dt), as the length of time from the Q-point of the ECG waveform to the B-point of the dZ/dt waveform (Berntson, Lozano, Chen, & Cacioppo, 2004).

Autonomic data were processed separately for a 5-minute baseline period and for the four blocks of the dichotic listening task. Data processing was performed using Mindware HF-HRV and IMP softwares (Gahanna, OH). First, ECG signals were

¹ This analysis plan was preregistered on 05/17/16 (<https://osf.io/xqncj/>).

inspected by trained research assistants to ensure the correct identification of individual R peaks. Edited ECG files were then used for the processing of PEP values, whereby visual inspection was used to verify that both the Q- and B- points were present and correctly placed in 30-second averages of ECG and dz/dt waveforms. HF-HRV, PEP, heart rate, and respiration rate values were exported in 30-second epochs, then averaged across epochs to yield a single baseline value and a separate value for each of the four blocks of the dichotic listening task. Physiological reactivity values during the task were calculated for all measures as difference scores from baseline values (task minus baseline). For HF-HRV, positive reactivity scores index greater PNS activation and negative scores index PNS withdrawal, relative to baseline levels. Because longer PEP intervals reflect less SNS activation, positive PEP change scores reflect SNS withdrawal during the task, and negative PEP change scores reflect SNS activation during the task, relative to baseline.

Procedure

Upon arrival to the laboratory, informed consent was obtained and electrode application was initiated. First, electrodes for the recording of ECG and IC were placed onto the participant's torso, followed by placement of an electrode cap and electrodes for EEG recording. During this time, electrodes for monitoring of ECG, IC, and EEG were also being placed onto the participant's child (reported elsewhere). Then, the participant and their child were ushered into an electrically-shielded, sound-attenuating booth for the baseline physiology recording. Children were seated in a comfortable chair positioned 145 cm away from a computer monitor, with two speakers placed 90° to the left and right of the chair, while parents were seated in a chair to the right of the child. Then, an initial five-minute "baseline" measure of ECG and IC were taken while a video depicting

calming ocean scenes and featuring low volume instrumental music was presented on the monitor. After the ocean video completed, a research assistant entered and ushered the parent out and into another booth down the hallway. A research assistant followed the parent into the new booth for initiation of the EEG recording, where parents were seated in a chair positioned 145 cm away from a computer monitor, with two speakers placed 90° to the left and right of the chair. Participants first heard instructions, followed by four stories with three open-ended comprehension questions asked in between each story to ensure participant attention to the task. After completion of the task, participants moved on to complete additional testing procedures (not reported here).

Results

Characterizing physiological reactivity to the selective attention task

Descriptive statistics for all physiological measures are shown in Table 1. Paired-sample *t*-tests of baseline and task values for HF-HRV, PEP, heart rate, and respiration rate showed significant task reactivity for all measures. HF-HRV power declined from baseline ($M = 6.09$, $SD = 1.13$) to task ($M = 5.98$, $SD = 1.06$), $t(92) = 2.01$, $p = .047$. PEP values shortened from baseline ($M = 113.93$, $SD = 10.95$) to task ($M = 112.88$, $SD = 10.65$), $t(92) = 2.02$, $p = .047$. These changes in HF-HRV and PEP were associated with concurrent slowing of heart rate from baseline ($M = 73.15$, $SD = 10.27$) to task ($M = 71.87$, $SD = 9.66$), $t(92) = 3.23$, $p = .002$, and acceleration of respiration rate from baseline ($M = 15.84$, $SD = 1.82$) to task ($M = 17.35$, $SD = 2.36$), $t(92) = -7.56$, $p < .001$.

Figure 2.1. *HF-HRV and PEP Values Across the Laboratory Visit.*

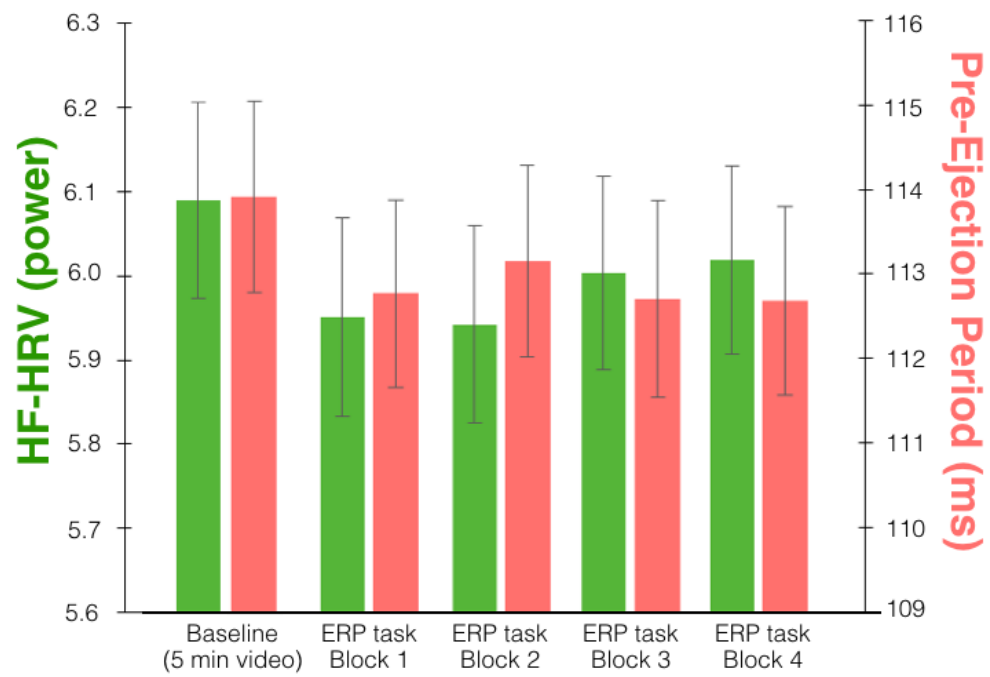


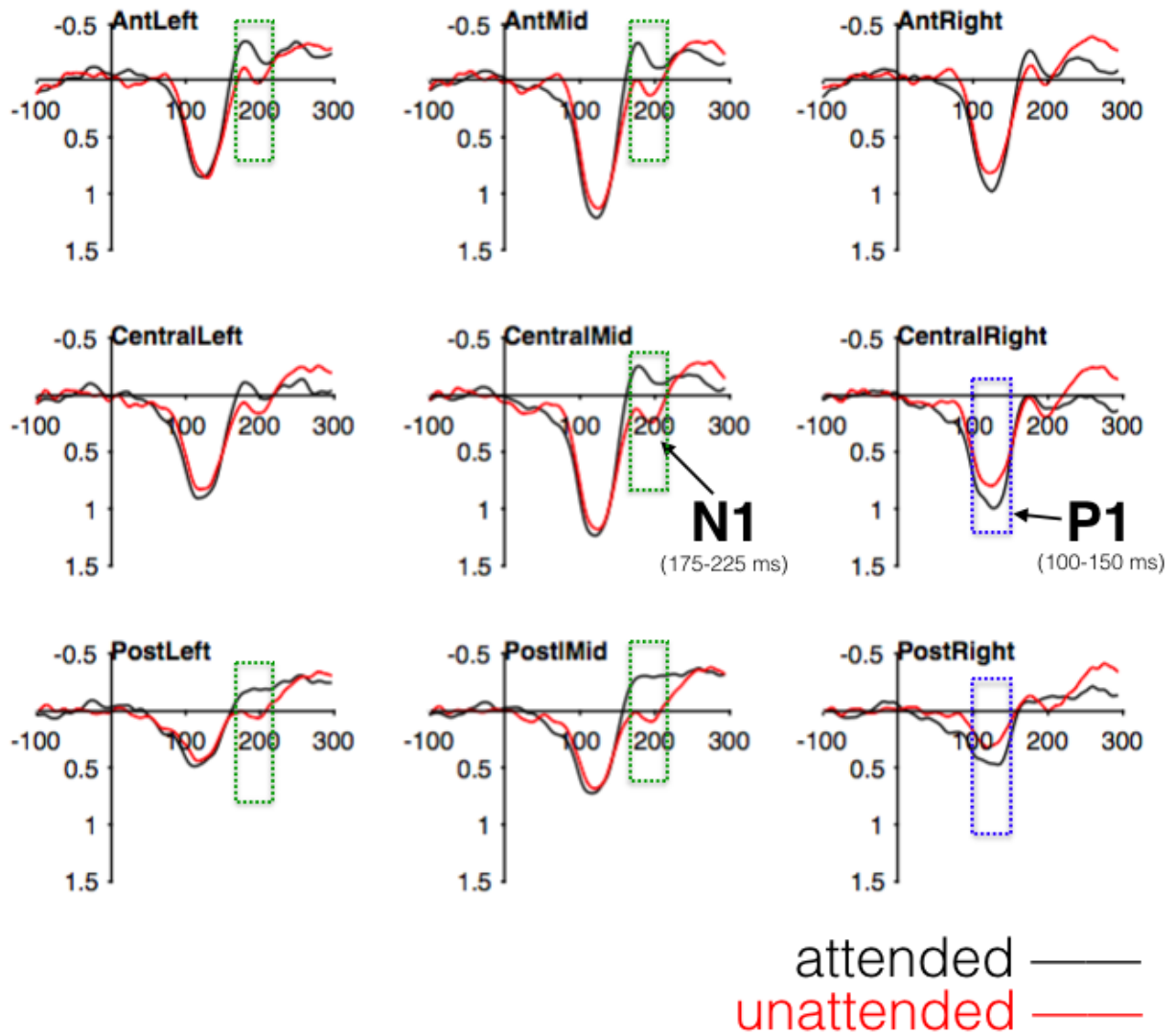
Table 2.1. *Descriptive Statistics for Age, SES, and Physiological Measures.*

	<i>M</i>	<i>SD</i>	Range
Participant age	32.56	7.51	22–67
SES risk factors	1.02	0.88	0–3
Baseline HF-HRV	6.09	1.13	3.28–8.52
Task HF-HRV	5.98	1.06	2.97–8.36
HF-HRV reactivity	-0.11	0.50	–2.12–1.15
Baseline PEP	113.93	10.95	87.80–143.60
Task PEP	112.88	10.65	87.82–139.61
PEP reactivity	-1.05	5.02	–10.81–16.15
Baseline heart rate	73.15	10.27	50.21–103.97
Task heart rate	71.87	9.66	52.23–97.18
Heart rate reactivity	-1.27	3.81	-9.89–8.49
Baseline respiration rate	15.84	1.82	11.70–21.66
Task respiration rate	17.35	2.36	12.18–24.55
Respiration rate reactivity	1.51	1.92	-4.40–8.33

Characterizing effects of selective attention on ERPs

Visual inspection of ERP waveforms elicited by sound probes embedded in attended and unattended narratives can be seen in Figure 1. For both probe conditions, a frontocentral maximum positive deflection can be seen peaking after 100 ms (“P1”), followed by a phasic negative deflection peaking before 200 ms (“N1”). Statistical analyses were performed separately on mean amplitudes extracted from ERPs in 50 ms windows centered on the P1 and N1 peaks, 100-150 ms and 175-225 ms respectively. For P1 mean amplitudes, results revealed an interaction of attention x laterality, $F(2, 184) = 3.41, p = .037$, such that significant effects of attention were seen at right-lateralized electrode clusters ($p = .020$) but not at left-lateralized or midline clusters ($ps > .35$). Follow-up comparisons showed that significant effects of attention on P1 amplitudes at the group level were seen at the right medial ($p = .009$) and right posterior ($p = .037$) electrode clusters. For N1 mean amplitudes, results revealed a main effect of attention, $F(1, 92) = 7.25, p = .008$, as well as an interaction of attention x laterality, $F(2, 184) = 11.36, p < .001$, such that significant effects of attention were seen at left-lateralized ($p = .007$) and midline electrode clusters ($p < .001$) but not at the right-lateralized clusters ($p = .553$). Follow-up comparisons demonstrated significant attention effects on N1 amplitudes broadly across the scalp [left anterior, $p = .027$; central anterior, $p = .012$; central midline, $p = .001$; left posterior, $p = .003$; midline posterior, $p < .001$]. Therefore, subsequent analyses quantified P1 amplitudes as a composite of the right medial and right posterior electrode clusters, while N1 amplitudes were quantified as a composite of the left anterior, midline anterior, midline central, left posterior, and midline posterior electrode clusters.

Figure 2.2. ERPs elicited by attended and unattended probes ($N=93$).



Associations between physiology and ERP effects of selective attention

Correlations amongst all variables of interest for subsequent analyses are shown in Table 2. Below, these results and follow-up analyses are presented separately for each ERP component. Notably, there were no significant associations between SES risk factors and any of the autonomic or ERP measures. Therefore, SES risk was not included in the following analyses.

Table 2.2. *Zero-order Correlations Among All Variables of Interest.*

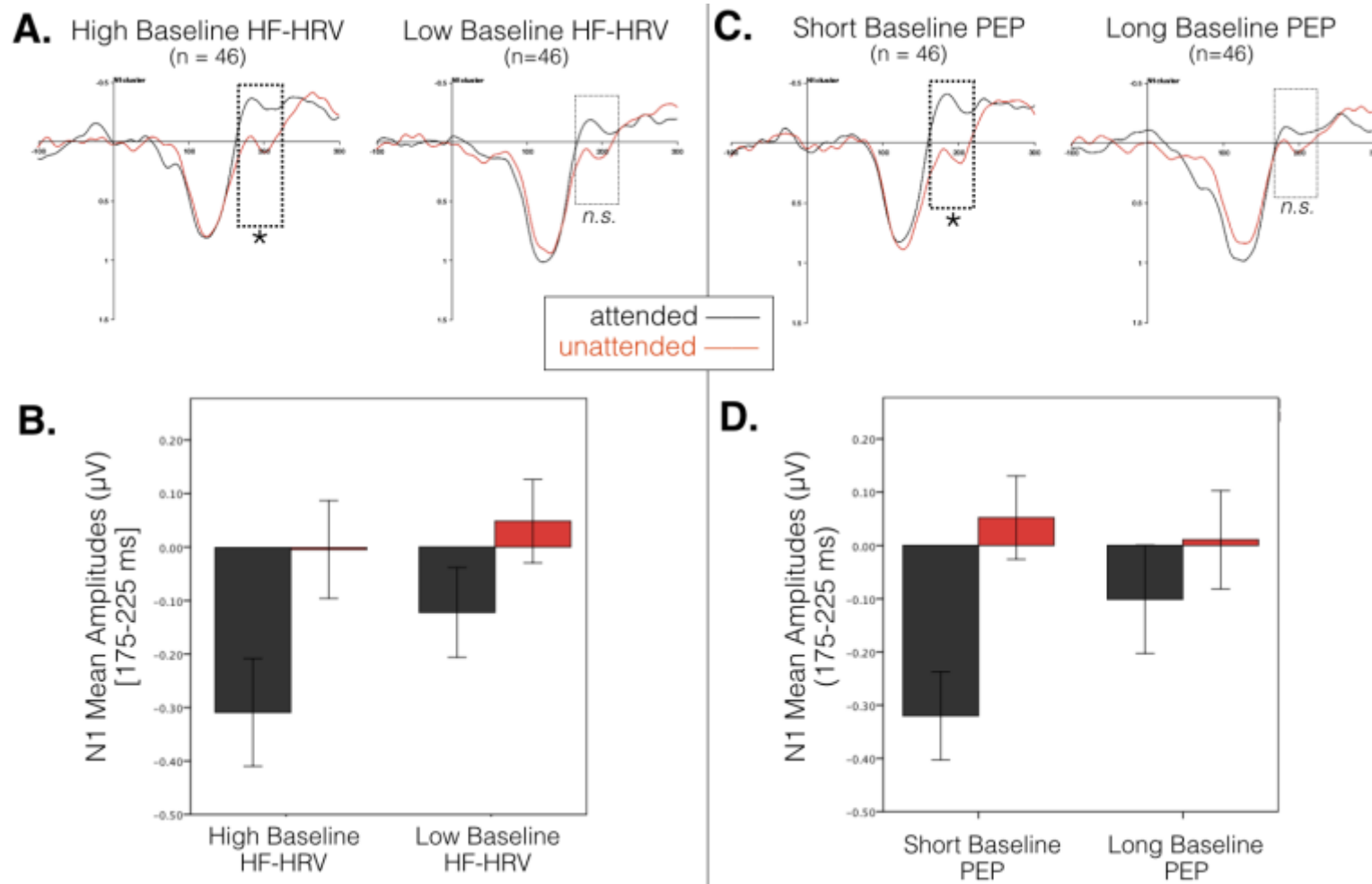
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Age	-													
2. SES risks	-.10	-												
3. HF-HRV baseline	-.37**	.09	-											
4. HF-HRV task	-.35**	.01	.90**	-										
5. HF-HRV reactivity	.10	-.18	-.35**	.11	-									
6. PEP baseline	.03	-.03	.05	.09	.09	-								
7. PEP task	.11	-.10	-.01	.03	.08	.89**	-							
8. PEP reactivity	.18	-.15	-.12	-.14	-.04*	-.29*	.18	-						
9. Attended P1 amp.	.17	.04	-.11	-.16	-.08	.17	.09	-.19	-					
10. Unattended P1 amp.	<.01	.17	-.14	-.14	.03	.08	.04	-.09	.32**	-				
11. Att. – Unatt. P1 amp.	.15	-.11	.02	-.03	-.10	.09	.05	-.09	.63**	-.54**	-			
12. Attended N1 amp.	.20	.02	-.25*	-.22*	.10	.25*	.31**	.10	.06	<.01	.06	-		
13. Unattended N1 amp.	.08	.09	<.01	-.01	-.01	-.01	-.01	<.01	-.14	.20	-.28**	.47**	-	
14. Att.- Unatt. N1 amp.	.13	-.07	-.25*	-.21*	.11	.26*	.32**	.10	.19	-.18	.32**	.58**	-.45**	-

P1 component (100-150 ms). No significant associations were observed between effects of attention on P1 amplitudes and measures of HF-HRV [baseline HF-HRV: $r(90) = .08, p = .459$; task HF-HRV: $r(90) = .02, p = .822$; HF-HRV reactivity: $r(90) = -.12, p = .271$] or measures of PEP [baseline PEP: $r(90) = .08, p = .425$; task PEP: $r(90) = .03, p = .767$; PEP reactivity: $r(90) = -.12, p = .255$].

N1 component (175-225 ms). Partial correlations controlling for age revealed significant associations between effects of selective attention on N1 amplitudes and both baseline HF-HRV, $r(90) = -.22, p = .037$, and baseline PEP, $r(90) = .26, p = .011$. A similar effect was observed between N1 amplitudes and task values of PEP, $r(90) = .31, p = .003$, although there was only a trend of N1 amplitudes correlating with baseline HF-HRV, $r(90) = -.18, p = .086$. As seen in Figure 2.3, higher baseline HF-HRV and shorter baseline PEP were associated with a larger effect of selective attention on N1 amplitudes. Notably, these effects remained when controlling for respiration rate [baseline HF-HRV, $r(90) = -.21, p = .046$; baseline PEP, $r(90) = .26, p = .013$]². Follow-up analyses of attended and unattended ERPs separately suggested that the relationship between baseline physiology and the N1 attention effect was driven by associations specific to attended ERPs. Shorter baseline PEP was associated with larger negative amplitudes to attended ERPs, $r(90) = .25, p = .015$, and a similar trend was observed between higher baseline HF-HRV and larger negative amplitudes to attended ERPs, $r(90) = -.19, p = .066$. There was no evidence of associations between baseline physiology and unattended ERPs ($ps > .79$).

² Effects of selective attention on N1 amplitudes were not significantly associated with baseline heart rate ($p = .715$), heart rate reactivity ($p = .592$), baseline respiration rate ($p = .826$), or respiration rate reactivity ($p = .440$).

Figure 2.3. ERPs by median split on baseline HF-HRV and baseline PEP.



Linear regression models were then performed to clarify the joint contributions of baseline HF-HRV and baseline PEP with effects of selective attention on N1 amplitudes, while controlling for reactivity values and age. As shown in Table 2.3, the effect of attention on N1 amplitudes was predicted by baseline HF-HRV and baseline PEP [$R^2 = .14$, $F(3, 89) = 4.80$, $p = .004$], with unique variance accounted for by baseline HF-HRV [$\beta = -.25$, $p = .021$] and baseline PEP [$\beta = .27$, $p = .007$]. Adding reactivity values of HF-HRV and PEP did not contribute additional explained variance to the model [R^2 change = .02, F change(2, 87) = 1.26, $p = .289$]. To test for interactions between baseline HF-HRV and PEP, an additional model was performed including an interaction term of baseline HF-HRV x baseline PEP, but adding the interaction term did not contribute additional explained variance [R^2 change = .02, F change(1, 86) = 1.80, $p = .183$]. In summary, the N1 attention effect showed a negative correlation with baseline HF-HRV and a positive correlation with baseline PEP: larger attention effects on the N1 component were associated with both greater baseline HF-HRV and shorter baseline PEP.

Table 2.3. *Regression models predicting the effect of selective attention on N1 amplitudes from baseline HF-HRV and PEP.*

Model 1			Model 2			Model 3		
	β	p		β	p		β	p
Age	.03	.766	Age	<.01	.977	Age	-.01	.896
Baseline PEP	.27	.007**	Baseline PEP	.32	.002**	Baseline PEP	.31	.004**
Baseline HF-HRV	-.25	.021*	Baseline HF-HRV	-.24	.033*	Baseline HF-HRV	-.26	.026*
			PEP reactivity	.17	.117	PEP reactivity	.16	.126
			HF-HRV reactivity	<.01	.996	HF-HRV reactivity	.02	.856
						Baseline PEP x HF-HRV	-.13	.183
Model fit, $F(3, 89) = 4.80, p = .004^{**}$			Model fit, $F(5, 87) = 3.40, p = .007^{**}$			Model fit, $F(6, 86) = 3.16, p = .008^{**}$		
$R^2 = .139$			F change (2, 87) = 1.26, $p = .289$			F change (1, 86) = 1.80, $p = .183$		
			$R^2 = .163$			$R^2 = .181$		

As an additional control, we examined whether associations between ERPs and autonomic physiology were confounded by the number of artifact-free trials available for ERP averaging. Zero-order correlations demonstrated a significant negative correlation between the number of artifact-free trials and baseline HF-HRV, $r(91) = -.33, p = .001$, such that higher baseline HF-HRV was associated with fewer artifact-free trials. No relationships were observed between artifact-free trials and HF-HRV reactivity ($p = .387$) or any measure of PEP (all $ps > .31$). Partial correlations between the N1 attention effect and baseline HF-HRV and baseline PEP were examined, while controlling for number of artifact-free trials. Significant relationships were still observed between the N1 attention effect and baseline HF-HRV, $r(90) = -.21, p = .042$, and between the N1 attention effect and baseline PEP, $r(90) = .29, p = .006$.

Discussion

This study sought to characterize the extent to which ERP mechanisms of selective attention are associated with markers of parasympathetic and sympathetic function, specifically HF-HRV and PEP, in a sample of adults from lower SES backgrounds. We observed a widely-distributed effect of selective attention on ERP amplitudes at the N1 component that was associated with baseline levels of HF-HRV and PEP. As predicted, individuals with higher baseline HF-HRV and shorter baseline PEP showed larger effects of selective attention. No relationship between current SES and autonomic physiology or ERPs was observed. These results demonstrate the importance of both autonomic branches for neural activity and cognitive performance, such that physiological components of flexible engagement and reward-sensitivity may be independent dimensions contributing to optimal neurocognitive function.

Consistent with a number of studies within the neurovisceral integration framework demonstrating a positive association between resting PNS activity and cognitive measures of attention (for a review, see Park & Thayer, 2014), greater baseline HF-HRV was associated with larger effects of selective attention on ERPs. Greater variability in high-frequency bandwidth of heart rate at rest has been proposed to reflect a greater capacity for self-regulation and cognitive performance, and underlying activity in the prefrontal cortex related to goal-directed behavior (Smith, Thayer, Khalsa, & Lane, 2017). Indeed, lesions to the prefrontal cortex have been associated with marked attenuations of the N1 attention effect in the selective attention used here (Knight, Hillyard, Woods, & Neville, 1981), suggesting that individuals with lower resting HF-HRV in the current study might also be individuals who exhibit less goal-directed activity (e.g. top-down control signals) in networks involving the prefrontal cortex.

Larger selective attention effects on ERPs were also associated with shorter resting PEP intervals, consistent with a number of previous studies finding positive associations between SNS activity and brain function (Beissner et al., 2013; Hajcak et al., 2003; 2004). In a review of autonomic influences on attention performance, Hugdahl noted that an increased galvanic skin response often accompanies sustained orienting and habituation to repeated stimuli, particularly with regard to demands for attentional control (Hugdahl, 1996). Interestingly, a similar relationship between increased galvanic skin response and higher-order cognitive processes has been proposed by several researchers (Edelberg, 1993; Tranel & Damasio, 1994; Ohman, 1992). In particular, given that lesions to the prefrontal cortex have been associated with an elimination of the galvanic skin response to attention-demanding stimuli (Tranel & Damasio, 1994), the SNS seems

similarly important for selective attention as the PNS. Yet, many reports of relationships between autonomic activity and attention only report measures of HF-HRV or heart rate (e.g., Park et al., 2013; 2014; Williams et al., 2016), suggesting that interpretations of the relationship between autonomic activity and attention may be biased towards PNS contributions to attention. For example, interpretations from studies employing PNS-mediated measures such as HF-HRV have emphasized the role of top-down regulation in attentional control (Park & Thayer, 2014), while interpretations based on studies employing SNS measures such as galvanic skin response have emphasized the role of bottom-up orienting responses (e.g., Hugdahl, 1996).

Considering the simultaneous contributions of resting HF-HRV and PEP to effects of selective attention observed here lends support for both views of autonomic contributions to attention, but leads to a more nuanced interpretation than would have likely been reached from either measure either autonomic system in isolation. When considering that higher resting HF-HRV is associated with better selective attention, this supports literature suggesting these same adults with higher HF-HRV have a greater capacity for regulation of behavior and attention. One interpretation of why this relationship exists might be that adults with higher resting PNS activation are calmer when they start the attention task, and that calm state may facilitate better selective attention to the stories of interest within the crowded environment. However, this interpretation seems unlikely when considering PEP, as larger attention effects were associated with shorter resting PEP, or greater sympathetic activation. A similarly short-sighted conclusion might be drawn from considering PEP in isolation, such that a more aroused and SNS-activated state might be seen as better for selective attention

performance. Considering both autonomic systems in tandem leads to a more refined interpretation: given evidence that shorter PEP reflects greater reward-related SNS activity as opposed to threat-related SNS activity (e.g., Brenner & Beauchaine, 2011), the phenotype of high resting HF-HRV and shorter resting PEP may reflect a general disposition of high self-regulation in the context of high approach-related behaviors. It is still possible that greater threat-related SNS arousal is indeed related to better selective attention performance, but this result must still be considered within the context of heightened PNS activity showing a similar relationship with attention. Given previous evidence that optimal behavioral performance is typically observed with reciprocally-activating systems (Melis & van Boxtel, 2001; 2007), the interpretation consistent with reciprocal activity suggests the shorter PEP observed here in the context of higher HF-HRV is due to shorter PEP indexing greater reward-related approach to the laboratory visit. This interpretation is also consistent with the experimental context of the selective attention task used here, where participants are asked to sit calmly without exposure to additional stressors or threats.

One limitation to the interpretation of the present findings is that the baseline physiological measurement was taken while adults were seated with their child in the ERP booth. While joint parent-child baseline measurements are often used in studies involving participants who are parents (e.g. Giuliano, Skowron, & Berkman, 2015), it is possible that adults in this study were actively engaged in self-regulation and parenting during the baseline measurement in order to facilitate their children sitting still and quiet through the 5-minute baseline video. If so, the baseline measure of HF-HRV may capture some degree of resting HF-HRV levels in addition to augmented HF-HRV to the extent

that individuals were engaged in regulated parenting (Skowron, Cipriano-Essel, Benjamin, Pincus, & Van Ryzin, 2013). Although less is known about how PEP during the act of parenting, baseline PEP values may be similarly biased. However, given that similar associations were observed between task values of HF-HRV and PEP with ERP attention effects, when the parents was in a separate room from their child, this explanation seems unlikely.

Another limitation to the present study concerns the generalizability of the findings based on a sample of adults living at-risk for a variety of poverty-related stressors. However, there is already a large body of research on higher SES populations, and researchers have called for studies with more diverse samples in psychophysical studies (Gatzke-Kopp, 2016). This sample is of particular relevance given efforts of translational science to harness the neuroplasticity of selective attention mechanisms in parenting programs (e.g., Neville et al., 2013). Thus, it is critical to characterize the relationship between attention and measures of autonomic physiology in individuals who would most likely be recruited for such family training programs. Even if the associations between autonomic physiology and selective attention reported here are unique to a lower SES population, this information is still very relevant for the evidence basis for intervention science, and suggests that targeting influences on autonomic physiology might facilitate efforts to train selective attention.

The lack of correlations between measures of HF-HRV and PEP observed here replicates a wide body of work demonstrating that the responses of the two autonomic branches represent separate dimensions of cardiac regulation (Berntson, Cacioppo, & Quigley, 1993b; Berntson et al., 1994; Berntson, Cacioppo, & Fieldstone, 1996).

Consistent with our own work, the two autonomic branches as indexed by HF-HRV and PEP appear to make unique contributions to cognitive function (Giuliano, Gatzke-Kopp, Roos, & Skowron, 2017). What remains to be seen is to what extent cognitive processing is related to reward-related versus threat-related measures of the SNS. Future studies should examine PEP in addition to electrodermal measures of galvanic skin response and examine the extent to which these measures index distinct contributions to neurocognitive processes.

Future research should extend the present methodology to a wider array of experimental tasks, and examine more dynamic measures of HF-HRV and PEP. ERPs in the present study are averaged from a relatively large number of stimulus events that are largely overlapping in time, which prohibits looking at single trial dynamics that have been shown to be sensitive to associations between ERPs and cardiac physiology (Mueller, Stemmler, & Wacker, 2010). Tasks measuring ERPs during response inhibition such as the Go/No-Go and Stop Signal tasks, provide an ideal opportunity to examine whether HF-HRV and PEP interact with brain activity on the scale of milliseconds (Hajcak et al., 2003), as opposed to associating broadly at the task level. Future research will also examine growth models of HF-HRV and PEP across the four blocks of the selective attention task and the extent to which growth dynamics are associated with ERP attention effects.

In summary, these results implicate both PNS and SNS activity in individual differences in neural mechanisms of auditory selective attention. Adults who showed higher resting levels of HF-HRV and shorter resting levels of PEP showed larger effects of selective attention at the N1 component. While these findings should be interpreted

with caution given the higher-risk nature of the sample, results suggest that more efficient selective attention function is associated with heightened PNS activity and reward-related SNS activity. Given that we observe individual differences in autonomic physiology to be associated with brain activity on a task designed to control for individual differences in arousal, this raises the possibility that a variety of group-level effects commonly reported in cognitive studies would also show interactions with individual participants' physiological state. While the present findings advocate for the inclusion of SNS measures alongside PNS measures of HF-HRV, future studies should specifically examine where electrodermal measures of SNS activity derived from skin conductance and cardiac measures of SNS activity indexed by PEP make unique contributions to neurocognitive processes.

CHAPTER III

EFFECTS OF EARLY ADVERSITY ON NEURAL MECHANISMS OF DISTRACTOR SUPPRESSION ARE MEDIATED BY SYMPATHETIC NERVOUS SYSTEM ACTIVITY IN PRESCHOOL-AGED CHILDREN

This work is currently undergoing peer review for publication and was co-authored with C.M. Karns, L.E. Roos, T.A. Bell, S. Petersen, E.A. Skowron, H.J. Neville, & E. Pakulak. I was the lead author of this chapter and the manuscript submitted for peer review. I established the study design, experimental methods, and data analyses with input and assistance from co-authors.

Introduction

Selective attention is a foundational skill for cognitive performance, implicated in learning (Blair & Razza, 2007), memory (Cowan et al., 2005), executive function (Garon, Bryson, & Smith, 2008), and school readiness (Duncan et al., 2007; Rueda, Checa, & Rothbart, 2010; Stevens & Bavelier, 2012). Given the severe capacity limits inherent in maintaining multiple units of information in mind while making decisions and judgments about that information, selective attention has been proposed to serve as a ‘gatekeeper’ mechanism for higher-order cognition, such that better performance on a variety of measures (e.g. working memory, fluid intelligence) is associated with the ability to efficiently allocate cognitive resources to relevant information while inhibiting the influence of irrelevant information (Awh & Vogel, 2008; Cowan, 2005; Fukuda, Vogel, Mayr, & Awh, 2010; Kane & Engle, 2002; Unsworth, Fukuda, Awh, Vogel, 2014).

Relative to other cognitive processes, mechanisms of selective attention show a remarkable degree of plasticity, malleable with changes in sensory experience and environmental demands (e.g., Neville & Lawson, 1987). However, the view of neuroplasticity as a double-edged sword predicts that these mechanisms of attention would also be more vulnerable in environments less supportive of their development (Stevens and Neville, 2013).

Early adversity and selective attention

Lower socioeconomic status (SES) early in life is one such environmental influence in which neural mechanisms supporting selective attention are vulnerable (D'Angiulli et al., 2012; Neville et al., 2013; Stevens, Lauinger, & Neville, 2009). It has been theorized that attentional deficits associated with lower SES are at least partly due to the impact of chronic stress on brain development (Neville et al., 2013), but very few studies have directly examined the association between neural measures of attention and biological measures of stress physiology. To date, one study has assessed selective attention and cortisol reactivity in children from lower SES backgrounds, and reported deficits in attention associated with lower SES but not cortisol reactivity (D'Angiulli et al., 2012). To our knowledge, no study to date has tested specific cardiac measures that can distinguish sympathetic (“fight-or-flight”) and parasympathetic (“rest-and-digest”) contributions to autonomic arousal. The present study addresses this gap in the literature by concurrently measuring event-related potentials and cardiac markers of autonomic physiology, specifically pre-ejection period and high-frequency heart rate variability indexing sympathetic and parasympathetic contributions respectively, during a selective attention task in a sample of lower SES preschool-aged children.

The preschool age is a developmental period associated with rapid neural and cognitive development, in particular for systems important for self-regulation (Brown & Jernigan, 2012), and we have found that event-related potentials (ERPs) provide a means to directly measure selective attention in children. Our story-based listening task does not require motor responses and is engaging to children as young as three years old (Coch, Sanders, & Neville, 2005; Sanders, Stevens, Coch, & Neville, 2006; Stevens, Lauinger, & Neville, 2009). It is based upon a robust ERP measure of selective attention, defined as the modulation of the neural response to sound probes embedded within to-be-attended narratives (termed ‘attended ERPs’) and to-be-unattended narratives (termed ‘unattended ERPs’) (Hillyard, Hink, Schwent, & Picton, 1973; Hillyard, Woldorff, Mangun, & Hansen, 1987; Woldorff & Hillyard, 1991) and is engaging across a range of ages (Karns, Isbell, Giuliano, & Neville, 2015).

Importantly, a subset of prior selective attention studies has documented deficits in neural measures of selective attention in children from lower SES backgrounds (Isbell, Wray, & Neville, 2015; Neville et al., 2013; Stevens, Lauinger, & Neville, 2009). These deficits are troubling given that individual differences in selective attention are associated with measures predictive of nonverbal intelligence in children (Isbell, Wray, & Neville, 2015) and adults (Giuliano, Karns, Neville, & Hillyard, 2014). If attention mechanisms are vulnerable in lower SES children, this could underlie school readiness disparities (e.g. Blair & Raver, 2015). However, this vulnerability of attention systems also provides an opportunity for intervention. We have demonstrated malleability of selective attention in lower SES children with an intervention that improves not only attention, but also self-reported parenting stress (Neville et al., 2013). In light of the vulnerability and

malleability of attention, is important to determine the role of stress in the relationship between early adversity and differences in attention mechanisms, to inform potential interventions in the critical early childhood years.

Early adversity, autonomic function, & cognition

A separate body of research has characterized the effects of early life stress on measures of the autonomic nervous system (ANS), documenting that both the sympathetic (SNS) and parasympathetic (PNS) branches of the ANS are profoundly impacted by experiences of early adversity (Propper & Holochwost, 2013). Heightened SNS activity has been observed as early as the *in utero* environment, where fetuses of mothers who report higher levels of perceived stress show higher resting heart rate (Allister, Lester, Carr, & Liu, 2001; DiPietro, Hodgson, Costigan, Hilton, & Johnson, 1996) and there is evidence of disrupted PNS activity in fetuses of mothers reporting higher levels of anxiety (Monk et al., 2004). Similar findings of reduced PNS activity have been reported in infants, with higher maternal depression or anxiety associated with reduced heart rate variability (Field, Pickens, Fox, Nawrocki, & Gonzalez, 1995; Jones et al., 1998; Ponirakis et al., 1998). In light of these findings, a key aim of the present study was to characterize the relationship between SES-related risk exposure and activity of the PNS and SNS in young children. Given evidence that coordination between both branches of the ANS is crucial for child outcomes in the face of adversity (El-Sheikh et al., 2009), we hypothesized that children exposed to a higher degree of low SES-related risk factors might rely more on the SNS relative to the PNS for adaptive function.

Importantly, both theory and behavioral findings implicate SNS and PNS activity as critical for healthy cognitive function, which raises the possibility that effects of early

life stress on neural measures of selective attention may be mediated by the ANS. The neurovisceral integration model (Thayer & Lane, 2000; 2009) suggests that activity of the ANS is important for higher-order cognitive function due to largely overlapping regions of the brain, such as the prefrontal cortex, implicated in both ANS regulation and cognition.

A small but growing body of research has emphasized links between the regulatory role of the PNS, indexed by high-frequency heart rate variability (HF-HRV; e.g., Berntson, Cacioppo, & Quigley, 1993a; Berntson & Cacioppo, 2004), and behavioral performance on cognitive tasks. In children, higher baseline HF-HRV, typically assessed while watching a calm video, has been linked to better performance on measures such as inhibitory control (e.g., Calkins, Graziano, & Keane, 2007). Additionally, a meta-analysis suggests that children showing greater HF-HRV withdrawal from baseline measures to task demands score higher on a variety of measures of cognitive-behavioral performance (Graziano & Derefinko, 2013). Notably, overall effect sizes linking PNS function to cognitive performance are small and often show varied patterns of associations in higher-risk samples (Conradt et al., 2016; Graziano & Derefinko, 2013; Skowron et al., 2014). Here, we employ HF-HRV withdrawal as a measure of PNS regulation and test its relationship with ERP measures of selective attention and exposure to adversity.

A literature primarily focused on adults has linked SNS function to behavioral and neural measures of cognitive performance (Hugdahl, 1996; Hajcak, McDonald, Simons, 2003; Hajcak, McDonald, & Simons, 2004), with less evidence regarding measures of SNS activity and cognitive outcomes in younger samples. A body of applied work has

implicated the SNS in self-regulation outcomes associated with conduct disorder and substance use (Beauchaine, Gatzke-Kopp, Neuhaus, Chipman, Reid, & Webster-Stratton, 2013; Brenner & Beauchaine, 2011; Hinnant, Erath, Tu, & El-Sheikh, 2015), such that young children who show reduced SNS reactivity at rest and in response to incentives score higher on measures of conduct problems and aggression (Beauchaine et al., 2013). Despite evidence that children show significant SNS reactivity to cognitive challenges even when controlling for motor task demands (Bush, Alkon, Obradovic, Stamperdahl, & Boyce, 2011), we are not aware of any studies that have systematically examined the contributions of the SNS to individual differences in cognitive performance in children. Here, we use measures of PEP at rest and a robust neural indicator of selective attention to test our hypothesis that SNS function relates to cognition in lower SES children.

Overall, there is growing evidence that early life adversity is linked to alterations in ANS function and that ANS function is linked to behavioral measures relevant to cognitive performance. However, few studies have examined how both PNS and SNS measures, when considered together, are related to early adversity or behavioral measures of cognition. Furthermore, we are not aware of any studies that have examined how neural mechanisms of cognition are related to PNS and SNS function, or whether early adversity impacts the relationship between brain function and PNS and SNS activity. The present study addresses these questions by characterizing SES-related alterations in SNS and PNS function and examining the extent to which these alterations mediate links between SES risk and neural measures of selective attention.

Current study

In the current study we test two main hypotheses related to early adversity. First, we hypothesized that exposure to more SES-related risk factors, such as low household income, low maternal education, and single parent status (Evans, Li, & Whipple, 2013), would be associated with differences in neural measures of children's auditory selective attention, specifically distractor suppression (Stevens et al., 2009). Second, we hypothesized that SES risk would be associated with altered SNS and PNS function, with greater risk associated with heightened SNS activity, indexed by shorter PEP, and reduced PNS activity, indexed by lower baseline values of HF-HRV and reduced HF-HRV withdrawal to the task.

Next, we tested the extent to which ANS regulation relates to neural measures of child attention. In terms of the PNS, we expected that higher baseline HF-HRV and greater HF-HRV withdrawal would be associated with larger effects of selective attention on ERPs, based on previous research emphasizing the role of HF-HRV in cognition (Beauchaine & Thayer, 2015; Graziano & Derefinko, 2013). However, given that altered relationships between HF-HRV and cognitive performance have been reported in samples of children at higher risk for exposure to chronic stress (Conradt et al., 2016; Skowron et al., 2014), we anticipated that SNS function would be related to neural measures of selective attention in this sample of predominantly lower SES children.

Finally, we tested a mediation model in which autonomic measures explain the relationship between early adversity, as measured by SES risk, and reduced selective attention, as measured by ERPs. These results extend the understanding of associations between early adversity, autonomic physiology, and selective attention in preschool-age children.

Method

Participants

Children and parents recruited for this study were currently enrolled in Head Start, and thus by definition from families living at or below the poverty line. Children were eligible to participate in laboratory visits if they were English language dominant, had no history of neurological impairment, and normal or corrected-to-normal vision. This research is part of a broader study in which we are testing the hypothesis that a two-generation training program integrated into Head Start services will positively impact stress physiology and brain function in children and parents. Electroencephalogram measures were successfully obtained from 123 children. Eight children were tested in Spanish and not included here. Of the remaining group, 13 children declined placement of electrodes for measurement of electrocardiogram (ECG), one child had unusable impedance cardiogram (IC) data due to excessive artifacts, and the caregiver of one child declined to report socioeconomic information. Therefore, final analyses included 100 children (50 females) ranging in age from 3-5 years old ($M = 4.31$, $SD = .54$, range = 3.18-5.37).

Measures

Socioeconomic status (SES) risk factors. We quantified SES-related risks using a cumulative approach with discrete, additive markers, specifically household income, maternal education, and maternal marital status (Evans & Kim, 2013). For each of the three indicators, risk was coded dichotomously as present (1) or not present (0), with each risk factor aimed to characterize the riskiest third of the sample for that dimension. Household income risk was quantified as households in the bottom third of annual

incomes within the sample, here annual incomes less than \$40,000 (N=55). Maternal education risk was quantified as households in which the mother's highest degree of education was a high school diploma or less (N=51). Marital status risk was quantified as single parent households, in this case all single-mothers (N=45). Descriptive statistics for overall SES risk are shown in Table 1.

Table 3.1. *Descriptive Statistics*

	<i>M</i>	<i>SD</i>	Range
Participant age	4.31	0.54	3.18–5.37
SES risk factors	1.08	0.92	0-3
Baseline HF-HRV	6.77	1.20	3.76–10.12
Task HF-HRV	6.80	1.20	4.01–9.74
HF-HRV reactivity	0.03	0.50	–1.32–1.48
Baseline PEP	83.33	8.52	61.40–103.10
Task PEP	83.85	8.28	61.88–104.96
PEP reactivity	0.59	2.34	–4.21–7.95
Attended ERP amplitudes	2.87	1.75	-2.20–6.68
Unattended ERP amplitudes	2.26	1.52	-0.91–6.36
Att. – Unatt. Amplitudes	0.61	2.03	-4.04–5.47

Auditory selective attention task. We used the same auditory attention ERP paradigm as our previous studies with child and adult participants (Karns, Isbell, Giuliano, & Neville, 2015; Neville et al., 2013; Stevens et al., 2009; Sanders et al., 2006;

Coch et al., 2005). Participants were cued to selectively attend to one of two simultaneously presented children's stories differing in location (left/right loudspeaker), narrator's voice (a male or female reading the entire story aloud), and content. Illustrations from the story being read from the attended loudspeaker were presented on a monitor. A green arrow pointing to the left or right was displayed on the monitor throughout each block to indicate the side of the to-be-attended narrative.

ERPs were recorded to 100 ms duration probe stimuli embedded in both to-be-attended and to-be-unattended narratives. Probe stimuli were either linguistic (a voiced syllable) or nonlinguistic (a broad spectrum buzz). The linguistic probe was the syllable /ba/, spoken by a female (a different voice from all the story narrators). The nonlinguistic probe was created by scrambling 4-6ms segments of the /ba/ stimulus, which preserved many of the acoustic properties of the linguistic probe. Across the stories, approximately 200 linguistic and 200 nonlinguistic probes were presented in each channel. The probes were presented randomly at an inter-stimulus interval (ISI) of either 200, 500, or 1000ms in one of the two loudspeakers at a time, with a range of plus or minus 25 ms of jitter for each ISI. The stories were presented at an average of 60 dB SPL, and the intensity of the probes was 70 dB. A researcher sat next to children throughout the task to ensure that they remained still and equidistant between the two loudspeakers, and to administer comprehension questions following each pair of simultaneously presented stories.

Within each testing session, a total of eight different stories were presented. Since two stories were presented simultaneously, there were a total of four listening blocks. The stories were selected from the following children's book series: *Blue Kangaroo* (Clark, 1998, 2000, 2002, 2003), *Harry the Dog* (Zion & Graham, 1956, 1960, 1965, 1976), Max

& Ruby (Wells, 1997, 2000, 2002, 2004), and *Munsch for Kids* (Munsch & Martchenko, 1989, 2001, 2002; Munsch & Suomalainen, 1995). In each of the four blocks, two stories were presented simultaneously with attention directed to the story played from either the left or right loudspeaker and read aloud by a different narrator from four narrators in total. For example, in one block, a participant could be directed to listen to the left loudspeaker, which might play a story read by a female narrator, while ignoring the right loudspeaker, which would be playing a story read by a male narrator; the illustrations on the monitor would correspond to the attended story. Each participant attended twice to a story on the right side and twice to a story on the left side, with start side counterbalanced across participants. For each participant, an individual narrator would be heard once as the narrator for an attended story and once as the narrator for an unattended story. After each story, an experimenter asked the participant three basic comprehension questions about the attended story to reinforce the goal of paying attention. The comprehension questions always had two alternatives. A response of “I don’t know” was counted as an incorrect response. As a criterion for inclusion in data analysis, participants answered a minimum of seven out of 12 questions correctly.

Electroencephalogram (EEG). During the dichotic listening task, EEG was recorded at a sampling rate of 512 Hz from 32 Ag/Ag-Cl-tipped scalp electrodes (BioSemi Active2, Amsterdam, Netherlands) arranged according to the international 10–20 system. Electrode offsets were maintained at ± 30 μ V or less throughout each recording session. Additional electrodes were placed on the outer canthus of each eye, below the right eye, and on the left and right mastoids. The EEG was recorded relative to the common mode sense active electrode and then re-referenced offline to the algebraic

mean of the left and right mastoids. Horizontal eye movements were plotted as the difference between the left and right outer canthus channels. Vertical eye movement, including eye blinks, were plotted as the difference between the lower right eye electrode and Fp1 (right anterior-most electrode). ERP analyses were carried out using EEGLAB (Delorme & Makeig, 2004) and ERPLAB (Lopez-Calderon & Luck, 2014). Raw EEG data were imported into EEGLAB and high-pass filtered at 0.1 Hz. Then, epochs time-locked to sound probes embedded in the dichotic listening task were extracted from –100 to 500 msec relative to probe onset. Epochs containing large voltage deviations or muscle/movement artifacts were identified by visual inspection and excluded from further analysis. Remaining data were then submitted to artifact rejection procedures within ERPLAB. Artifacts were identified based on moving window peak-to-peak changes in eye channels across a 200 ms window, moving in 50 ms increments. Individual artifact rejection parameters were adjusted for each subject to identify the smallest amplitude changes associated with eye movements or blinks. Manual artifact rejection was employed after the automatic ERPLAB procedures, to ensure accuracy of artifact marking. Following artifact rejection, epochs were low-pass filtered at 40 Hz.

In order to reduce the multiple comparisons that would be needed to model interactions between SES risk with HF-HRV and PEP both at baseline, during the task, and task reactivity, we reduced ERP data to a composite electrode representative of ERPs elicited across the scalp. Based on previous findings with the same dichotic listening task showing significant individual differences in ERPs at frontocentral electrodes sites (Giuliano, Karns, Neville, & Hillyard, 2014; Isbell, Wray, & Neville, 2015;), we calculated a composite electrode averaged across the 8 primary frontocentral electrode

sites (F3/F4, C3/4, Cp1/2, Fz, Cz.). Visual inspection of ERP waveforms elicited by sound probes embedded in attended and unattended narratives (see Supplemental Figure 1) confirms that the most pronounced ERPs are at frontocentral electrode sites. Statistical analyses were performed on mean amplitudes extracted from ERPs in a 50 ms window centered on the prominent positive deflection elicited by probes in both condition, 150-200 ms post probe onset. An attention (2) x electrode (32) repeated-measures ANOVA controlling for SES risk was performed to verify that significant effects of attention were observed in this time-window when considering all electrode sites. Results revealed a main effect of attention, $F(1, 98) = 7.89, p = .006$, and an interaction of attention x SES risk, $F(1, 98) = 7.33, p = .008$, suggesting that the 150-200 ms time window adequately represents group-level selective attention effects as well as individual differences associated with SES risk.

Cardiovascular physiology. A montage of 11 electrodes was used for the measurement of high-frequency heart rate variability (HF-HRV) and pre-ejection period (PEP). Electrocardiogram (ECG) was obtained from three disposable pre-gelled electrodes placed in a modified Lead II configuration on the distal right clavicle, lower left rib, and lower right abdomen. Impedance cardiogram (ICG; Z0) was recorded from eight electrodes placed in a tetrapolar configuration on the left and right lateral neck and torso, from a vertical maximum of the jawline down to the diaphragm. Data were acquired wirelessly via Biopac Nomadix BN-RSPEC and BN-NICO transmitters (Biopac Systems Inc, Goleta, CA) sending ECG and impedance signals respectively to a Biopac MP-150 acquisition unit placed in the room with the participant. A respiration signal was derived from the raw impedance cardiogram for the inspection of respiration values.

High-frequency HF-HRV values were derived from natural log-transformed values of the spectral power in the high frequency range commonly used for this age group (.24-1.04 Hz). PEP was calculated from the first-order derivative of the cardiovascular impedance signal (dZ/dt), as the length of time from the Q-point of the ECG waveform to the B-point of the dZ/dt waveform (Berntson, Lozano, Chen, & Cacioppo, 2004).

Autonomic data were processed separately for a 5-minute baseline period and for the four blocks of the dichotic listening task. Data processing was performed using Mindware HF-HRV and IMP softwares (Gahanna, OH). First, ECG signals were inspected by trained research assistants to ensure the correct identification of individual R peaks. Edited ECG files were then used for the processing of PEP values, whereby visual inspection was used to verify that both the Q- and B- points were present and correctly placed in 30-second averages of ECG and dZ/dt waveforms. HF-HRV and PEP values were exported in 30-second epochs, then averaged across epochs to yield a single baseline value and a separate value for each of the four blocks of the WM task. Physiological reactivity values during the dichotic listening task were calculated for both HF-HRV and PEP as difference scores from baseline values (task minus baseline), such that positive HF-HRV reactivity scores indexed greater PNS activation and negative scores indicated PNS withdrawal, relative to baseline levels. Because longer PEP intervals reflect less SNS activation, positive PEP change scores reflect SNS withdrawal during the task, and negative PEP change scores reflect SNS activation during the task, relative to baseline.

Procedure

Upon arrival to the laboratory, verbal informed consent was obtained from children and written assent provided by the child's parent. First, electrodes for the recording of ECG and IC were placed onto the child's torso, followed by placement of an electrode cap and electrodes for EEG recording. During this time, electrodes for monitoring of ECG, IC, and EEG were also being placed on parents (not reported here). Then, the child was ushered into an electrically-shielded, sound-attenuating booth with their parent. Children were seated in a comfortable chair positioned 145 cm away from a computer monitor, with two speakers placed 90° to the left and right of the chair. Parents were seated in a chair to the right of the child for an initial five-minute "baseline" measure. During this measure, a five-minute video depicting calming ocean scenes and featuring low volume instrumental music was presented on the monitor. After the ocean video completed, a research assistant entered the booth while the parent was ushered out of the booth and into another room. Once the research assistant was seated next to the child, the auditory attention task was initiated. At the end of the task, the electrode cap and other external EEG electrodes were removed, and children were allowed to pick a small toy out of a treasure chest as a reward for completing the task. Children were then ushered out of the EEG booth by the research assistant and lead to another room for additional testing procedures (not reported here).

Results

Descriptive statistics are shown in Table 1 and zero-order correlations among all variables are shown in Table 2. Participant age was positively correlated with measures of PEP at baseline [$r(98) = .36, p < .001$] and during the task [$r(98) = .35, p < .001$]. Therefore, age was entered as a covariate in all subsequent analyses.

Hypothesis 1: Early adversity impacts selective attention. SES risk was positively associated with mean amplitude of ERPs elicited by unattended probes during the dichotic listening task [$r(98) = .21, p = .037$], such that children with more risk factors showed a larger positive deflection in ERPs to distractor sounds. The increasing amplitude of unattended ERPs with the increasing accumulation of SES risk factors is illustrated in Figure 1. There were no significant relationships between SES risk and ERP amplitudes elicited by attended probes [$r(98) = .07, p = .485$] or the overall degree of attentional modulation on ERPs, indexed by difference scores of ERP amplitudes elicited by attended minus unattended probes [$r(98) = -.10, p = .335$].

Figure 3.1. *Event-Related Potentials (ERPs) as a function of SES risk exposure.*

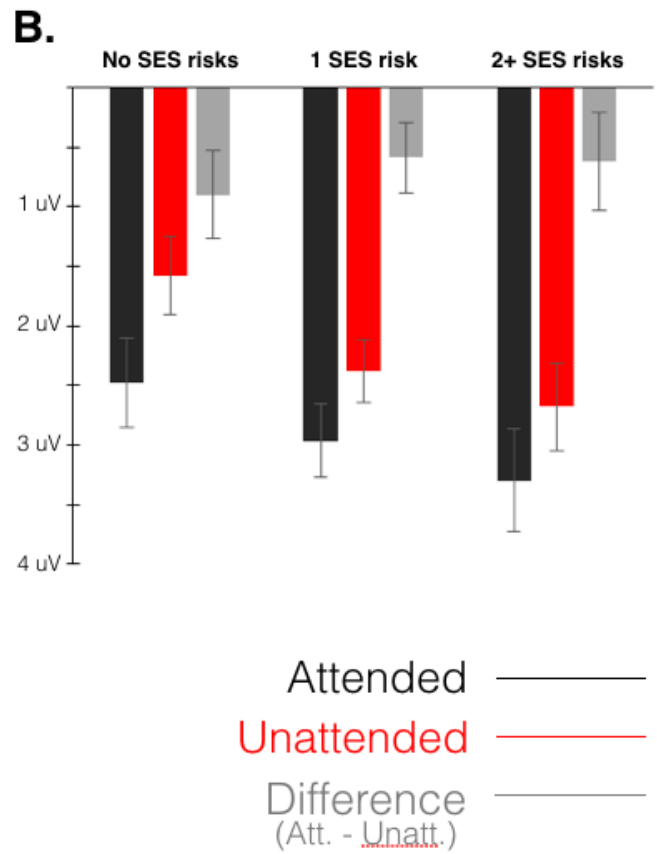
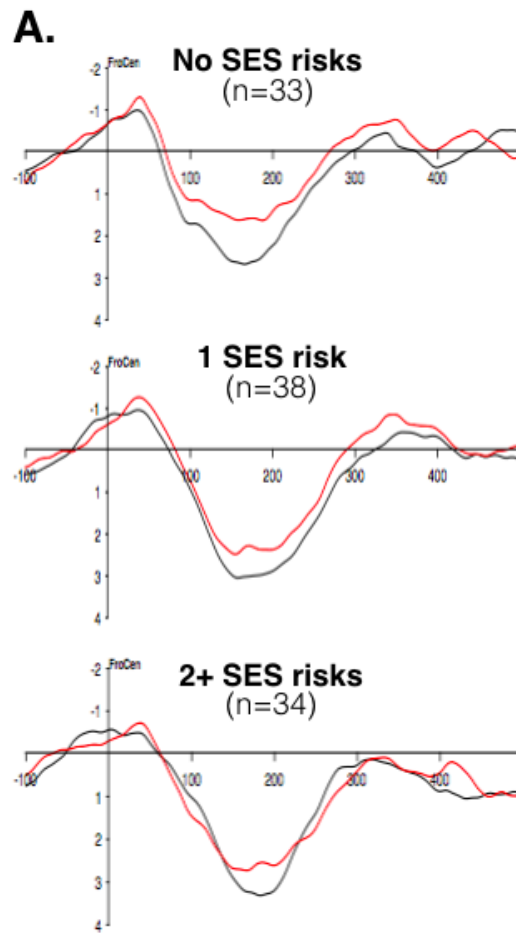


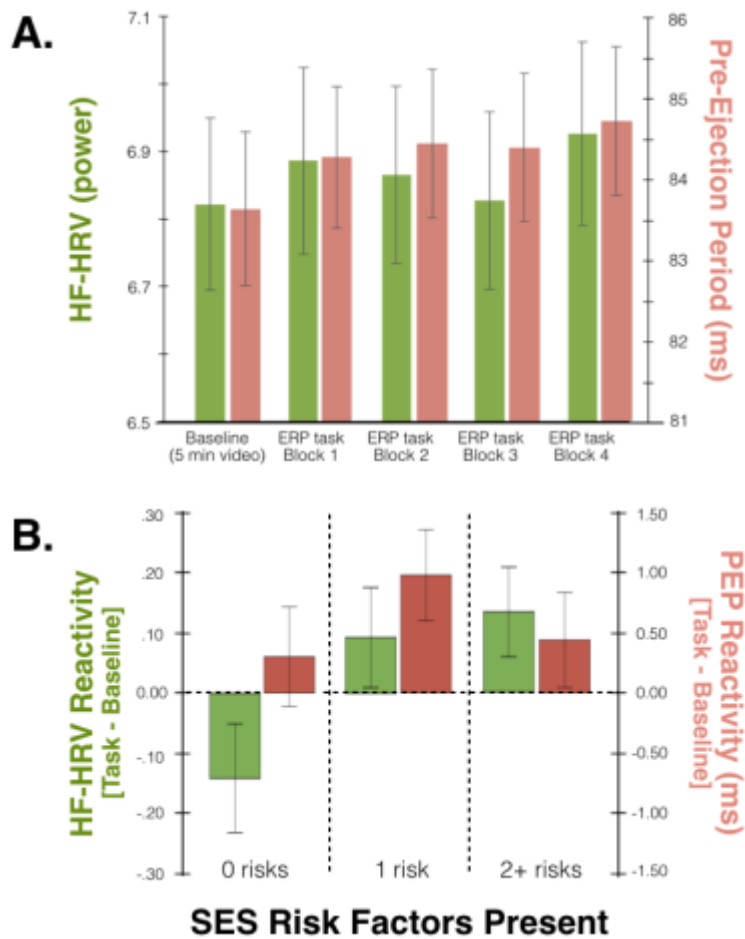
Table 3.2. *Zero-order Correlations Among All Variables of Interest.*

	1	2	3	4	5	6	7	8	9	10	11
1. Age	-										
2. SES risks	-.20	-									
3. Attended ERP amplitudes	.18	.07	-								
4. Unattended ERP amplitudes	-.01	.21*	.24*	-							
5. Attended – Unattended amplitudes	.16	-.10	.68**	-.55**	-						
6. HF-HRV baseline	.06	-.03	.02	.05	-.02	-					
7. HF-HRV task	.07	.07	.10	.08	.02	.91**	-				
8. HF-HRV reactivity	.05	.24*	.17	.07	.10	-.19	.235*	-			
9. PEP baseline	.36**	.14	.12	.29**	-.12	-.17	-.14	.06	-		
10. PEP task	.35**	.14	.15	.26*	-.06	-.15	-.12	.08	.96**	-	
11. PEP reactivity	-.07	-.02	.10	-.17	.21*	.09	.13	.09	-.27**	.01	-

** , $p < .01$; * , $p < .05$

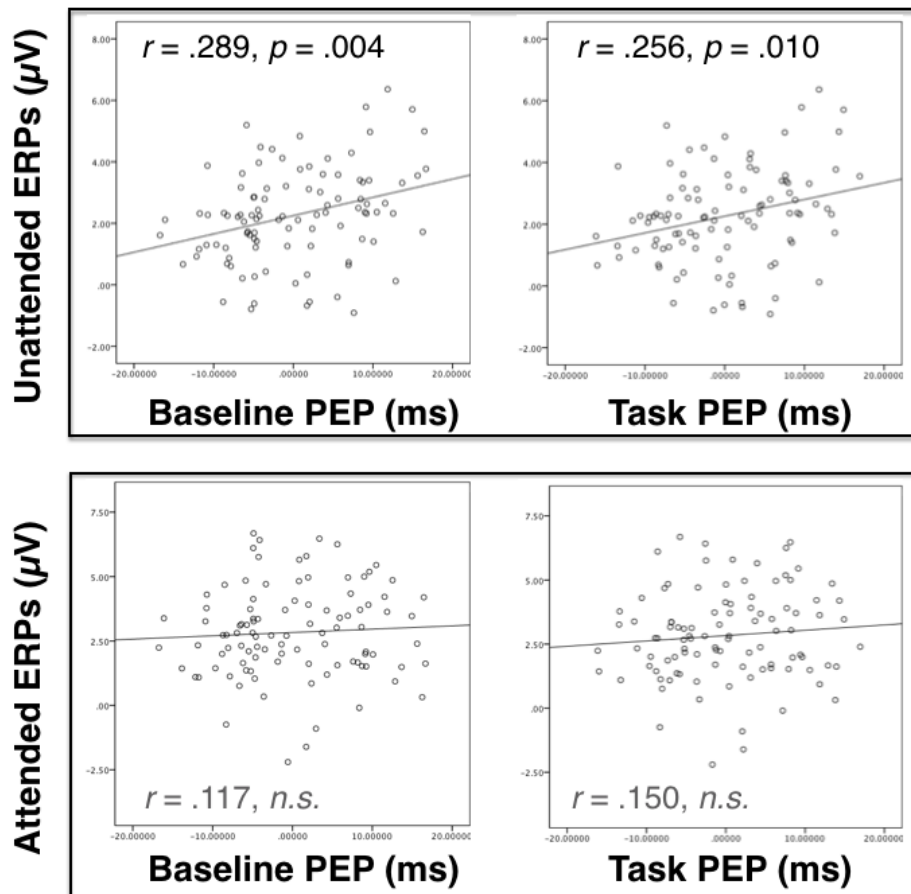
Hypothesis 2: Early adversity impacts autonomic function. In line with our hypothesis, the number of SES risk factors was positively associated with HF-HRV reactivity to the task [$r(98) = .24, p = .017$]. Examination of Figure 2 shows that children with no SES risk factors showed HF-HRV withdrawal to the task relative to baseline, while children with one or more risk factors showed HF-HRV augmentation to the task relative to baseline. In contrast, PEP reactivity (task versus baseline) was not systematically related to SES risk [$r(98) = -.02, p = .838$], nor were baseline and task levels of PEP related to SES ($ps > .16$).

Figure 3.2. *HF-HRV and PEP values during the visit and reactivity by SES risk.*



Hypothesis 3: Selective attention related to autonomic measures. Next we tested the relationship between the neural measures of selective attention and cardiac measures of the PNS and SNS. We found no relationships between measures of HF-HRV and ERPs, but unattended probe amplitudes were significantly related to baseline PEP [$r(98) = .29, p = .004$] and task PEP [$r(98) = .26, p = .010$] (Figure 3). Shorter PEP was associated with smaller ERPs amplitudes to unattended probes. We also observed a significant association between PEP reactivity and the difference of attended minus unattended ERP amplitudes [$r(98) = .21, p = .032$]. Larger overall effects of selective attention were observed in children who showed PEP elongation from baseline to task.

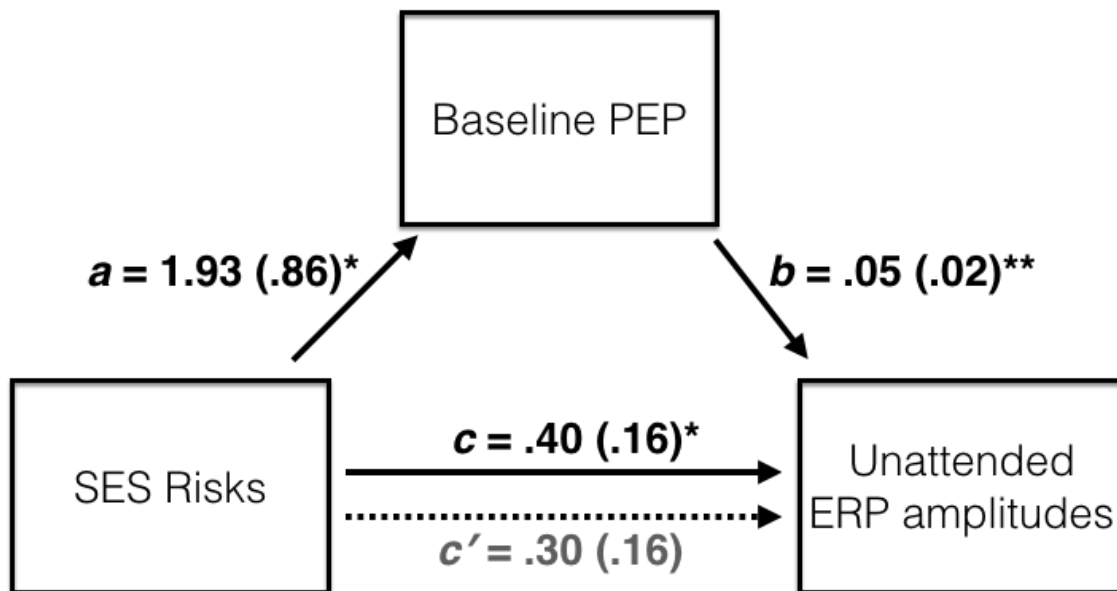
Figure 3.3. *Correlations between frontocentral aggregate ERPs and PEP values.*



Hypothesis 4: Autonomic measures mediate effect of adversity on attention.

Given that mean ERP amplitudes elicited by unattended probes were significantly associated with SES risk and PEP during baseline and task, we tested whether baseline PEP values mediated the relationship between SES risk and ERP amplitudes for unattended probes. Mediation was tested for baseline and task PEP in separate models using the PROCESS macro (v.2.16; Hayes, 2013) while controlling for child age. As shown in Figure 4, the relationship between SES risk and ERP amplitudes elicited by unattended probes was significantly mediated by baseline PEP ($B = .109$; 95% confidence interval [CI], .021-.259). The effect of SES risk on distractor ERPs ($B = .366$, $p = .035$) was no longer significant when considering baseline PEP ($B = .257$, $p = .134$). Nearly identical results were observed for the same model with task PEP as the mediator ($B = .095$; 95% CI, .016-.232).

Figure 3.4. *Mediation model of baseline PEP, SES risk exposure, and unattended ERPs.*



Next, we examined whether the significant association between HF-HRV reactivity and SES risk would account for additional variance in the above mediation models. Given our hypotheses about interactions between HF-HRV and PEP, we were interested in whether HF-HRV reactivity would interact with PEP in mediating the relationship between SES risk and distractor ERP amplitudes. This model specifically tested HF-HRV reactivity as a moderator of the path between baseline PEP and distractor ERP amplitudes in the previously described mediation model (PROCESS model 14). However, the interaction term of HF-HRV reactivity x baseline PEP was not significant in moderating the effect of baseline PEP on distractor ERP amplitudes ($B = -.06$; 95% CI, $-.144$ to $.015$; $p = .108$). A similar result was observed in the same model with task PEP ($B = -.07$; 95% CI, $-.153$ to $.013$; $p = .099$).

As an additional control, we examined whether associations between ERPs and autonomic physiology were confounded by the number of artifact-free trials available for ERP averaging. Zero-order correlations demonstrated a significant positive correlation between the number of artifact-free trials and baseline HF-HRV, $r(98) = .25$, $p = .012$, such that higher baseline HF-HRV was associated with a greater number of artifact-free trials. No relationships were observed between artifact-free trials and HF-HRV reactivity ($p = .664$) or any measure of PEP (all $ps > .25$). Furthermore, number of accepted trials was not associated with child age or SES risk exposure (both $ps > .47$). Partial correlations between ERP amplitudes elicited by distractors and PEP were examined, while controlling for number of artifact-free trials. Significant relationships were still observed between distractor ERP amplitudes and baseline PEP, $r(97) = .30$, $p = .002$, and between distractor ERP amplitudes and task PEP, $r(97) = .30$, $p = .003$.

Discussion

This study sought to characterize the extent to which deficits in neural mechanisms of selective attention, which are vulnerable in children from lower SES backgrounds, are related to autonomic measures of stress physiology. In a sample of children enrolled in Head Start, we showed that the accumulation of socioeconomic risk factors is associated with deficits in selective attention, indexed by larger ERP responses to distractor sounds in a dichotic listening environment, such that children from more risky backgrounds showed less suppression of the auditory response to distractor stimuli (Stevens et al., 2009). In line with other research (Skowron et al., 2014), we demonstrated that SES risk was also associated with autonomic nervous system functioning such that only children with no SES risk factors showed HF-HRV task withdrawal. Further, we extended these findings by showing that the effects of SES risk on distractor ERPs was mediated by activity of the SNS, as measured by PEP. Children with longer PEP at rest and during the task, indexing lower SNS arousal, showed less suppression of distractor sounds as indexed by larger unattended ERPs. These findings support basic tenets of the neurovisceral integration model regarding the interrelationship of neural and autonomic activity (Thayer & Lane, 2009), and demonstrate that associations between electrophysiological measures of brain activity and autonomic nervous system function are relevant for understanding the impact of chronic stress on cognitive processes. The relationship between long PEP and larger distractor ERPs may be related to findings that blunted SNS activity, indexed by elongated PEP, is a risk factor for children at relatively high risk for early adversity (Hinnant et al., 2016; Brenner & Beauchaine, 2011).

As noted, this study builds on a small body of research linking SES risk to neural measures of selective attention. In particular, we replicate the results of Stevens and colleagues (2009), who reported that differences in selective attention in 3-5 year old children from lower SES backgrounds were due to an enhancement of ERP amplitudes in response to unattended probes, suggesting deficits in the ability to suppress distracting information. However, that study had a relatively small sample size of lower SES children ($n=16$) and relied on maternal education as a proxy for low SES. Here, we replicate this finding in a larger sample of one-hundred 3-5 year old children enrolled in Head Start using a cumulative risk framework to characterize SES. We show that even within a predominantly lower SES sample, there are meaningful individual differences between the accumulation of SES-related risks and neural mechanisms of selective attention.

It is important to note that our findings do not speak to whether reduced distractor suppression is maladaptive in all contexts. Given findings that lower SES environments are more likely to be characterized by greater household chaos, including elevated noise levels and increased risk for exposure to violence (Evans & Kim, 2013), it may adaptive in home environments for children of lower SES households to not engage in the same degree of suppressing responses to ‘distractor’ stimuli as their higher SES peers (Blair & Raver, 2012). However, success in the classroom largely emphasizes the successful suppression of stimuli that may distract from focusing attention on a teacher’s voice or task at hand. Even within a large sample of children from predominantly lower SES backgrounds such as the current study, increasing exposure to SES-related risks is associated with increasingly attenuated distractor suppression during selective attention.

Thus, higher SES risk early in life may predispose children for academic failure via compromised selective attention performance that is more susceptible to the influence of distractors. The differences in selective attention observed here are relevant given that the current sample of children are all enrolled in Head Start, a program designed to improve school readiness. Given that selective attention is a foundational skill, improving school readiness in Head Start children may be best achieved by targeting the improved development of selective attention (Neville et al., 2013).

Next, we characterized the extent to which SES risk was related to the SNS and PNS measures during the baseline, task, and task reactivity. Higher SES risk was associated with longer PEP, suggesting reduced or ‘blunted’ SNS activity with increasing risk exposure. This is a surprising finding in light of previous reports in fetuses and infants that heightened maternal risk factors led to measures of heightened SNS arousal, but here the relationship between longer PEP and higher SES risk was apparent in both a resting baseline and task (story listening) conditions. Higher SES risk was also associated with blunted parasympathetic withdrawal from baseline to the task, which was seen as continued activation of the PNS during the attention task in children with exposure to SES risk factors (Figure 2). These results are consistent with theory and findings discussed in a comprehensive review by Propper and Holochwost (2013) that describes how early life stressors more common in children raised in lower SES environments (e.g., maternal stress, substance use during pregnancy, poor-quality parent–child interactions, and specific disruptions in parenting behavior) are associated with reduced PNS influences on cardiac function and heightened SNS influences on behavior. In the present study we see a similar altered pattern using a relatively simple measure of SES risk, in

the form of reduced HF-HRV withdrawal to the task and heightened SNS activity associated with better selective attention. These SES-linked alterations in PNS and SNS function are noteworthy given the already at-risk nature of a sample of children drawn from Head Start, a program for lower SES families. Future studies should examine larger samples with a wider representation of higher SES children, in order to better characterize patterns of ANS function as a function of the full spectrum of SES-related risks.

Finally, we determined whether the ANS profiles associated with SES risk accounted for links between SES and distractor suppression. Because PEP showed robust associations to both SES risk and distractor suppression, it was a prime candidate for such mediation. Baseline and task levels of PEP both fully mediated the effects of SES risk on distractor suppression. Although we cannot draw firm conclusions about causality given the cross-sectional nature of the present study, we offer two potential interpretations that should be followed up in future research. One interpretation is that the SES-linked alterations of both SNS function and selective attention are due to environmental impacts on shared mechanisms likely in prefrontal cortices (Thayer, Ahs, Fredrikson, Sollers, & Wager, 2012). This would be consistent with theories outlined emphasizing the role of attenuated SNS activity as a risk factor for the development of self-regulation (Beauchaine et al., 2013; Hinnant et al., 2016). Blunted SNS activity potentially indexes abnormal function of neural mechanisms associated with mesolimbic dopamine function (Brenner & Beauchaine, 2011), among which includes mechanisms of selective attention (e.g., Slagter et al., 2012). A second interpretation is that proximal stressful experiences, more common to children with SES risk, alter biological function

in both SNS and neural systems supporting selective attention in a parallel manner. For example, it is plausible that biological profiles supportive of high arousal and vigilance (i.e., high SNS and attention to ‘distractors’ that could be threatening) would be more common in children with high SES risk, but these systems would not necessarily be co-dependent (Del Giudice, Ellis & Shirtcliff, 2011; Propper & Holochwost, 2013). While we do not see heightened SNS activity associated with increasing SES risk, our results show that better selective attention performance is associated with heightened SNS activity in a sample of predominantly lower SES children. Regardless of causality, the findings that SNS activity mediates the link between SES risk and distractor suppression suggest a cross-system phenotype of biological function that has important implications for understanding why children from low SES backgrounds may be particularly at risk for lower cognitive function and associated outcomes such as school failure. More research is needed with children of a wider range early life experiences is needed to determine whether the SNS has a general role in cognitive function early in life.

Because HF-HRV reactivity was not associated with distractor suppression, we did not examine whether it mediated the effects of SES risk on distractor ERP amplitudes. However, given our primary interest in interacting systems, we examined whether HF-HRV moderated the association between PEP and distractor suppression in a moderated mediation model. We found no evidence of significant moderation by HF-HRV over and above the mediating impact of PEP. It may be that the range of SES was too small to detect moderated-mediation. At least two studies to date have shown that higher risk samples show PNS augmentation associated with better cognitive function (Conradt et al., 2016; Skowron et al., 2014). Consistent with this, in our own work we

have recently found evidence that links between PNS withdrawal and inhibitory control performance are only present in children with lower socioeconomic risk (Giuliano et al., under review). Alternatively, PNS function may only show associations with behavior in samples characterized by a wider range of SES. Evolutionary psychologists have also suggested that children exposed to early life stressors may develop more vigilant biological profiles characterized by SNS dominance with regard to behavior, in which the PNS may be blunted and less relevant for goal directed processes such as selective attention (Del Giudice et al., 2011). It is interesting that here we observe individual differences in neural mechanisms of selective attention primarily related to SNS function. This may be due to task demands that primarily emphasize staying alert and vigilant throughout each story. Additionally, given that the task only involves brief interactions with an experimenter between stories, this may result in minimal activation of so-called “social engagement systems” indexed by HF-HRV activity (Porges, 2007), thus placing less emphasis on the role of HF-HRV in this selective attention task.

Limitations of the study include that the sample is predominantly from lower SES backgrounds, thus the results reported here may not generalize to higher SES children. Future research will build on this work by sampling a wider range of SES. Another potential limitation of this study is that children were only included in analyses if they successfully completed the ERP measure of selective attention. Therefore, associations between PNS physiology and neural mechanisms of distractor suppression were examined in a sample of children who already had the regulatory capacity to tolerate electrode application and sit still for the length of the task. This type of sampling bias has been noted as a likely confound in a majority of studies on individual differences in

cognition early in life, particularly those studies involving the application of additional equipment for the monitoring of biomarkers (Gatzke-Kopp, 2016). It is possible that regulation of the ANS is even more crucial for children who are less likely to undergo such an experimental procedure. However, it should be noted that EEG involves a relatively less invasive measurement than other forms of neuroimaging, such as magnetic resonance imaging studies that require children to sit still while in a loud, space-restricted environment.

Taken together, these results provide the first documentation of links between ANS function and neural measures of selective attention. This is a critical first step in mapping out the potential role of neurovisceral integration theory (Thayer & Lane, 2009) as an explanatory tool towards better understanding the relationships between biological systems supporting cognitive function and adaptive outcomes. Given that here we report SNS activity as a full mediator of the impact of SES on selective attention, pathways identified as relevant to cognition in the neurovisceral integration model may serve as mechanisms through which early life stress “gets under the skin” to alter cognitive function (Hertzman & Boyce, 2010). Future research on longitudinal associations between early life stress and ANS function holds promise for continued efforts to identify important causal links between systems (e.g., Conradt et al., 2016), in particular the extent to which early adversity may causally impact children’s ANS function and selective attention, and whether or not healthy ANS function and/or selective attention may have protective effects biologically. Additionally, a more mechanistic understanding of these relationships can inform intervention research that can demonstrate to what

extent ANS mechanisms, and associations between the ANS and selective attention, may be malleable and improve with training.

We also note here that children with higher SES risk exposure were characterized by altered PNS reactivity. However, PNS reactivity was not associated with ERPs elicited by unattended distractors. Specifically, children with no risk factors showed HF-HRV withdrawal to the task, a common observation in ANS studies of child cognition (Graziano & Derefinko, 2013), while children with exposure to one or more risk factors showed HF-HRV augmentation to the task. These results are similar to others who have argued that children exposed to greater adversity may show HF-HRV augmentation to cognitive tasks, indexing engagement of the PNS, when attempting difficult cognitive tasks (Skowron et al., 2014). It is interesting that we see individual differences associated with HF-HRV reactivity here given the motor demands of the selective attention task here, which involve sitting quietly and not making manual responses, in contrast to other tasks that typically require children to be active and make speeded manual responses. This provides additional support to claims of the neurovisceral model regarding PNS withdrawal as a mechanism supporting the engagement of neural resources for cognitive function and not due to motor activity required to meet task demands (Thayer & Lane, 2009). It should be noted that significant changes in HF-HRV withdrawal were observed here, despite task demands of the baseline ocean video being closely matched to the task demands of the selective attention task, as recommended for studies of physiological reactivity in children (Bush et al., 2011). Future research should examine whether similar physiological profiles associated with early adversity are also related to neural mechanisms crucial for child cognition, such as inhibitory control.

In conclusion, these results provide strong support for existing theories linking early adversity to altered selective attention abilities early in life, while offering new explanatory mechanisms for such results. Specifically, our results suggest that the effects of lower SES on young children's deficits in selectively focusing attention are accounted for by chronic activation of the SNS. Children with relatively blunted SNS activity, indexed by longer pre-ejection times in measures of PEP, may be at heightened risk for deficits in distractor suppression commonly observed in lower SES children. Children showing heightened SNS activity may be better at suppressing distractor information. This study is the first in a systematic line of research investigating the contributions of autonomic physiology to the development of neural mechanisms of cognition in children. As shown here, such studies are likely to be particularly informative for understanding cognitive development in children at risk for exposure to a high degree of early life stressors.

CHAPTER IV

GENERAL DISCUSSION

Overview

In the following discussion, results for children and adults are summarized and interpreted in regards to the neurovisceral integration model. Given that the findings of both experiments are discussed extensively in Chapters II and III, the summary provided here largely focuses on notable similarities and differences between the two chapters. Limitations of the present findings are then presented, including a variety of alternate interpretations to the pattern of results observed. This section is concluded by a discussion of future directions, focusing on the refinement of measurement techniques for capturing more temporally-precise dynamics in autonomic activity and the importance of extending this body of research to more demographically-diverse samples.

Summary and Implications

The primary aim of this dissertation was to systematically assess the contributions of both autonomic branches to neural mechanisms of selective attention in children and adults. An additional aim was to examine whether the presence of risk factors associated with chronic stress exposure would impact measures of autonomic and brain function, and, if so, whether autonomic function would mediate the effects of chronic stress on brain function.

For both adults and children, SNS function as measured by PEP was associated with neural mechanisms of selective attention. Shorter PEP during baseline periods and the selective attention task were associated with larger overall effects of selective attention in adults, and greater suppression of distractor ERPs in children. These findings

are consistent with studies implicating SNS activity in the orienting response and sustained attention (Hugdahl, 1996), and neuroimaging results that have found associations between SNS function and activity in regions of the brain classically associated with attention, such as the amygdala, basal forebrain, and prefrontal cortex (Beissner et al., 2013). It is possible that increased SNS activity, indexed by PEP, serves to increase the salience of the auditory information being selectively attended to, via bottom-up influences on attention networks in the brain. Accordingly, reward-related SNS activity, indexed by PEP, may be critical for basic attention, learning, and memory functions. Given that populations exposed to early adversity are frequently documented to exhibit blunted reward-related function, measures of SNS activity may be particularly relevant for understanding alterations in cognitive function (Beauchaine, Gatzke-Kopp, & Mead, 2007; Beauchaine et al., 2013; Brenner & Beauchaine, 2011). Future studies should characterize the contributions of PEP alongside electrodermal measures such as galvanic skin response to neurocognitive measures in order to determine whether reward- and threat-related SNS activity make differential contributions to higher-order brain functions such as selective attention.

PNS activity was only related to selective attention in adults and not children. Notably, this association was in the direction predicted by the neurovisceral integration model, such that greater resting HF-HRV was associated with a larger N1 attention effect. When considering the lack of association between HF-HRV and selective attention in children, it is worth noting that the association between HF-HRV and selective attention in adults was relatively small compared to the association between PEP and attention. Regardless, resting HF-HRV was significantly associated with adult selective

attention, demonstrating that adults with greater PNS activity while watching a video with their child have larger effects of selective attention on their ERPs. In the limitations below, potential confounds during the baseline period are addressed concerning the social nature of measuring adult resting physiology while they are with their child in an observed context. In particular, it is possible that HF-HRV during the baseline period was only associated with ERPs for adults because adults might have been more likely to be engaged in socioemotional regulation during the baseline than children were.

When factoring in exposure to chronic stress, the presence of a greater number of SES-related risk factors for children was associated with longer resting PEP values and an exaggerated ERP response to distractor sounds in children. No relationship was observed between risk factors and biological measures in adults. A mediation model demonstrated that the effect of increasing risk exposure on larger distractor ERPs in children was fully accounted for by the effects of risk exposure on PEP activity at rest and during the task. These findings suggest that relationship between SNS activity and cognitive function may be disrupted as a function of early adversity, and serve as a contributing factor to the attentional profile more frequently observed in children from lower SES backgrounds. These findings may be particularly meaningful for understanding other aspects of cognition in poverty-exposed children given that altered profiles of selective attention effects on ERPs in this task have been associated with deficits in working memory and executive function performance in both adults and children (Giuliano, Karns, Neville, & Hillyard, 2014; Isbel, Wray, & Neville, 2015). It is similarly critical to investigate whether changes in SNS mechanisms indexed by PEP are associated with improvements in selective attention effects on ERPs that have previously

been reported in children enrolled in a parent-child intervention targeting the improvement of school readiness skills (Neville et al., 2013). The lack of a relationship between measures of current SES risk exposure and autonomic function or ERPs in adults may be due to sampling from a restricted range of SES. Alternatively, it could be due to the fact that risk exposure was only collected for adult's present-day status, and not during the early childhood period which is believed to be a sensitive and influential time for the 'programming' of stress regulatory systems such as SNS (Del Giudice, Ellis, & Shirtcliff, 2011). These limitations are elaborated upon below.

Limitations

A primary limitation to the interpretability of the present findings concerns the sample of children and adult participants recruited, who were recruited primarily from lower SES backgrounds. However, there is already a large body of research on higher SES populations, and researchers have called for studies with more diverse samples in psychophysical studies (Gatzke-Kopp, 2016). This sample is of particular relevance given efforts of translational science to impact selective attention performance in preschool-aged children, often including attentional training for both children and their parents (e.g., Neville et al., 2013). Thus, it is critical to characterize the relationship between attention and measures of autonomic physiology in both children and adults who would most likely be recruited for such family training programs. Even if the associations between autonomic physiology and selective attention reported here are unique to a lower SES population, this information is still very relevant for translational science, and suggests that targeting influences on autonomic physiology might facilitate efforts to train selective attention.

One major flaw of the experimental design of both experiments is that the baseline physiological measurement involves different demand characteristics for adults and children, who were assessed together. During the five-minute baseline recording, adults were likely engaged in parenting their children in order to meet the experimenter-requested demands of: sitting still, having minimal contact with electrodes, and remaining relatively quiet throughout a video of ocean scenes. At this point in the experimental protocol, children had just been ushered into a radio-frequency shielded EEG booth, while wearing numerous electrodes on their torso, head, and face, and were asked to sit still and not talk while watching the five-minute ocean video. Based on previous research with parent-child dyads, we would expect the demands of this context to lead to relatively higher values of HF-HRV for parents, as they are actively engaged in regulating their self and child, and relatively lower values of HF-HRV for children, who are in a novel context attempting an age-appropriate attention-demanding task. For adults, the degree of increase in HF-HRV values for adults would be expected to scale with the degree of positive parenting that adult was engaged in (Skowron et al., 2013), thus the association between higher resting HF-HRV and attention may reflect individual differences in underlying parenting characteristics. Future studies should include additional baseline measures where adults and children are measured separately, and when adults and children are measured together. Video-coded observations would offer valuable information in understanding individual differences in parenting behaviors during the baseline dyadic assessment.

The lack of robust associations between physiological reactivity and ERPs may be due to inadequately capturing task reactivity. It is likely that using a single value of HF-

HRV and PEP to quantify approximately 15 minutes of task activity is missing information related to dynamics in the physiological response. As such, the results reported here concerning resting and task level measures of HF-HRV and PEP likely reflect more trait-like characteristics across individuals (Beauchaine, 2001). Below we describe a number of future directions for more adequately quantifying state-like autonomic activity.

Future Directions

The results presented here represent the initial efforts to establish associations between autonomic activity and brain function. Analyses utilized single values of HF-HRV and PEP averaged across a 5-minute period for baseline values, and averaged across an approximately 15-minute period for task values. Although we did not see relationships between brain activity and reactivity of HF-HRV and PEP from baseline to task, this could be due to quantifying a 15-minute task period by a single value. A number of studies have shown that growth models of autonomic physiology across 30-second epochs are more sensitive to individual differences than simple difference scores of task minus baseline activity (e.g., Brooker & Buss, 2010; Giuliano, Skowron, & Berkman, 2015). Based on previous findings and neurovisceral integration theory, it could be predicted that individuals who show greater dynamic range in their HF-HRV and PEP (i.e. greater variability in values from block to block), would show larger effects of selective attention. Similarly, the dynamic range of HF-HRV and PEP can be examined during the 5-minute baseline period to more accurately quantify within individual dynamics (Fisher, Reeves, & Chi, 2016).

Extending this measure to other ERP paradigms, such as measures of inhibitory control, would allow for the examination of associations with HF-HRV and PEP on a single-trial level. The cardiac-encephalographic covariance tracing method has been used to demonstrate single-trial associations between heart rate and ERP amplitudes which vary in strength as a function of individual differences in anxiety and trial type (Mueller, Stemmler & Wacker, 2010; Mueller, Stemmler, Hennig, & Wacker, 2013). It is of particular interest to apply this methodology to ERP studies of inhibitory control in children and adults by examining single-trial covariance across multiple autonomic markers, including heart rate and PEP, in association with ERP components associated with stimulus attention, error-monitoring, and feedback processing. These studies will examine the central hypothesis that chronic stress exposure impacts flexible autonomic contributions to concurrent neurocognitive function on a trial-by-trial basis, and allow us to examine interactions between physiology and brain function for multiple cognitive processes represented by distinct ERP components.

Further, applying novel measures of autonomic and neural covariation holds particular promise for explaining the high degree of variability observed across populations. For example, broad relationships between HF-HRV, cognition, and resting brain activity show inconsistencies between Caucasian-americans and African-americans (Jennings et al., 2014). More temporally-precise measures of covariation between brain activity, PNS, and SNS activity would enable the examination of whether different populations show different profiles of neurovisceral integration and allow for a high degree of functional specificity to different task contexts. Given that a much of the psychophysiological literature is based on research with university students (Gatzke-

Kopp, 2016), our fundamental ideas of how the autonomic nervous system scaffolds behavior may be biased towards individuals who are relatively high SES, with relatively low exposure to chronic stressors. Specifically, studies of university samples might be biased towards individuals with higher resting HF-HRV, for whom the dynamic range of HF-HRV would also be greater (Berntson, Cacioppo, & Quigley, 1993b), while studies that include adults from backgrounds of higher risk for exposure to chronic stressors might involve a different dynamic range of HF-HRV and SNS measures. By recruiting individuals with a more diverse array of life experiences, future research can characterize the full spectrum of autonomic space, wherein the result of interactions between PNS and SNS activity may be particular to an individual's balance in PNS-SNS space.

Concluding Remarks

The two studies presented here demonstrate an association between heightened SNS activity and larger effects of selective attention on ERPs in adults and children. In children, the association between SNS activity and ERP measures of selective attention accounted for disparities in selective attention associated with increasing SES risk factor exposure. While the measure of SNS activity used here implicates greater reward-related processing as an important factor in more optimal selective attention, future studies should extend these findings to include threat-related measures of SNS activity (i.e. galvanic skin response). Ultimately, these findings raise the possibility that targeting function of the autonomic nervous system, in particular reward-related aspects of the SNS, may be one potential mechanism by which to leverage attempts to train and improve selective attention skills in children and adults.

APPENDIX A: SUPPLEMENTAL RESULTS FOR CHAPTER 2

Due to the small number of males ($n=6$) in the overall sample, results reported in the main manuscript are replicated here with females only ($N=87$). Any differences in findings between the two analyses are summarized in a final section, at the end of the results below.

Characterizing physiological reactivity to the selective attention task

Paired-sample t -tests of baseline and task values for HF-HRV, PEP, heart rate, and respiration rate showed significant task reactivity for all measures. HF-HRV power declined from baseline ($M = 6.12$, $SD = 1.12$) to task ($M = 6.00$, $SD = 1.08$), $t(86) = 2.44$, $p = .017$. PEP values shortened from baseline ($M = 113.57$, $SD = 10.08$) to task ($M = 112.40$, $SD = 10.28$), $t(86) = 2.45$, $p = .016$. These changes in HF-HRV and PEP were associated with concurrent slowing of heart rate from baseline ($M = 73.61$, $SD = 10.39$) to task ($M = 72.27$, $SD = 9.80$), $t(86) = 3.22$, $p = .002$, and acceleration of respiration rate from baseline ($M = 15.82$, $SD = 1.84$) to task ($M = 17.33$, $SD = 2.35$), $t(86) = -7.54$, $p < .001$.

Characterizing effects of selective attention on ERPs

For P1 mean amplitudes, results revealed an interaction of attention x laterality, $F(2, 172) = 3.95$, $p = .023$, such that significant effects of attention were seen at right-lateralized electrode clusters ($p = .033$) but not at left-lateralized or midline clusters ($ps > .57$). Follow-up comparisons showed that significant effects of attention on P1 amplitudes at the group level were seen at the right medial ($p = .019$) and right posterior ($p = .047$) electrode clusters.

For N1 mean amplitudes, results revealed a main effect of attention, $F(1, 86) = 8.06, p = .006$, as well as an interaction of attention x laterality, $F(2, 172) = 12.61, p < .001$, such that significant effects of attention were seen at left-lateralized ($p = .002$) and midline electrode clusters ($p < .001$) but not at the right-lateralized clusters ($p = .588$). Follow-up comparisons demonstrated significant attention effects on N1 amplitudes broadly across the scalp [left anterior, $p = .015$; central anterior, $p = .012$; left central, $p = .024$; central midline, $p = .001$; left posterior, $p = .001$; midline posterior, $p < .001$].

Associations between physiology and ERP effects of selective attention

Correlations amongst all variables of interest for subsequent analyses are shown in Supplemental Table 1. Below, these results and follow-up analyses are presented separately for each ERP component. Notably, there were no significant associations between SES risk factors and any of the autonomic or ERP measures. Therefore, SES risk was not included in the following analyses.

P1 component (100-150 ms). No significant associations were observed between effects of attention on P1 amplitudes and measures of HF-HRV [baseline HF-HRV: $r(84) = .08, p = .478$; task HF-HRV: $r(84) = .02, p = .885$; HF-HRV reactivity: $r(84) = -.14, p = .199$] or measures of PEP [baseline PEP: $r(84) = .07, p = .525$; task PEP: $r(84) = .03, p = .818$; PEP reactivity: $r(84) = -.10, p = .364$].

N1 component (175-225 ms). A significant association was observed between effects of selective attention on N1 amplitudes and baseline PEP, $r(84) = .23, p = .035$, with a similar effect observed between N1 amplitudes and task values of PEP, $r(84) = .27, p = .014$. There was a marginal trend of N1 amplitudes correlating with baseline HF-HRV, $r(84) = -.21, p = .058$. Shorter baseline PEP and higher baseline HF-HRV were

associated with a larger effect of selective attention on N1 amplitudes. Notably, the directionality of these effects remained when controlling for respiration rate [baseline PEP, $r(83) = .22, p = .044$; baseline HF-HRV, $r(83) = -.20, p = .072$]³. Follow-up analyses of attended and unattended ERPs separately suggested that the relationship between baseline physiology and the N1 attention effect was driven by associations specific to attended ERPs. Shorter baseline PEP was associated with larger negative amplitudes to attended ERPs, $r(83) = .23, p = .034$, and although higher baseline HF-HRV was associated with larger negative amplitudes to attended ERPs, this relationship was non-significant, $r(83) = -.18, p = .106$. There was no evidence of associations between baseline physiology and unattended ERPs ($ps > .85$).

Linear regression models were then run to clarify the joint contributions of baseline HF-HRV and baseline PEP with effects of selective attention on N1 amplitudes, while controlling for reactivity values and age. As shown in Supplemental Table 2, the effect of attention on N1 amplitudes was significantly predicted by baseline HF-HRV and baseline PEP [$R^2 = .14, F(3, 83) = 3.62, p = .016$], with unique variance accounted for by baseline HF-HRV [$\beta = -.23, p = .045$] and baseline PEP [$\beta = .23, p = .027$]. Adding reactivity values of HF-HRV and PEP did not contribute additional explained variance to the model [R^2 change = .02, F change(2, 81) = .96, $p = .387$]. To test for interactions between baseline HF-HRV and PEP, an additional model was performed including an interaction term of baseline HF-HRV x baseline PEP, but adding the interaction term did

³ Effects of selective attention on N1 amplitudes were not significantly associated with baseline heart rate ($p = .437$), heart rate reactivity ($p = .553$), baseline respiration rate ($p = .814$), or respiration rate reactivity ($p = .397$).

not contribute additional explained variance [R^2 change = .03, F change(1, 80) = 2.50, p = .118].

Summary of analyses after excluding male participants

Overall, there was a high degree of overlap between results for the full sample (N=93) and results for the sample when only females were considered (N=87). The same pattern of physiological reactivity was observed across HF-HRV, PEP, heart rate, and respiration rate, with very similar raw values for each measure between the two samples. Analyses of the attention effect at the P1 and N1 components were nearly identical, with the lone exception being an additional electrode cluster showing a significant N1 attention effect with the female-only sample (left central, p = .024), which was only marginally associated in the full sample (left central, p = .058).

Associations between the ERP attention effect, HF-HRV, and PEP were also very similar to analyses with the full sample. Both analyses showed no relationship between HF-HRV or PEP with the P1 attention effect, while baseline HF-HRV and PEP showed associations with the N1 attention effect. Although the association between baseline HF-HRV and the N1 attention effect was relatively attenuated in the female-only sample, $r(84) = -.21$, $p = .058$, relative to the full sample, $r(90) = -.22$, $p = .037$, when entering both baseline HF-HRV and baseline PEP into the model together with age, baseline HF-HRV remained a significant predictor of the N1 attention effect along with baseline PEP.

Table S1. *Zero-order Correlations Among All Variables of Interest for Female Adults.*

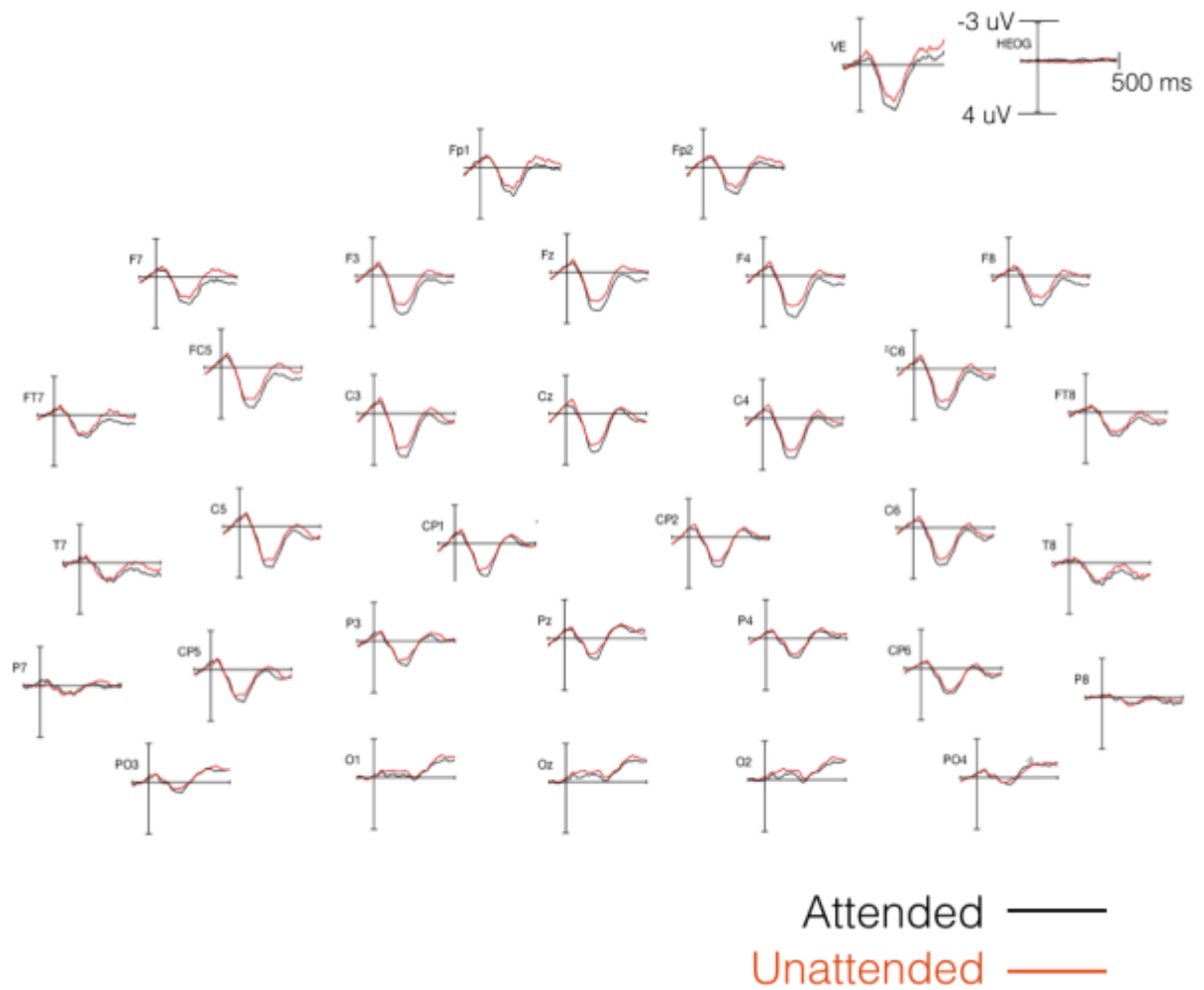
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Age	-													
2. SES risks	-.09	-												
3. HF-HRV baseline	-.37**	.06	-											
4. HF-HRV task	-.35**	-.01	.91**	-										
5. HF-HRV reactivity	.07	-.17	-.30**	.12	-									
6. PEP baseline	.10	.01	-.01	.08	.20	-								
7. PEP task	.13	-.06	-.01	.04	.11	.90**	-							
8. PEP reactivity	.09	-.14	-.01	-.10	-.20	-.18*	.26	-						
9. Attended P1 amp.	.19	.04	-.13	-.18	-.09	.17	.09	-.16	-					
10. Unattended P1 amp.	.01	.17	-.16	-.14	.06	.08	.05	-.07	.31**	-				
11. Att. – Unatt. P1 amp.	.16	-.10	.02	-.04	-.13	.08	.05	-.08	.63**	-.55**	-			
12. Attended N1 amp.	.23*	.05	-.25*	-.21*	.12	.25*	.29**	.12	.07	<.01	.06	-		
13. Unattended N1 amp.	.09	.09	-.01	-.01	.01	.01	.02	.02	-.15	.19	-.28**	.48**	-	
14. Att.- Unatt. N1 amp.	.14	-.03	-.24*	-.20*	.11	.24*	.28**	.10	.21	-.18	.33**	.57**	-.45**	-

Table S2. *Regression Model Predicting the Effect of Selective Attention on N1 Amplitudes from Baseline HF-HRV and PEP for Female Adults.*

Model 1			Model 2			Model 3		
	β	p		β	p		β	p
Age	.04	.736	Age	.02	.844	Age	-.01	.962
Baseline PEP	.23	.027*	Baseline PEP	.26	.019*	Baseline PEP	.23	.033*
Baseline HF-HRV	-.23	.045*	Baseline HF-HRV	-.22	.059	Baseline HF-HRV	-.24	.043*
			PEP reactivity	.15	.170	PEP reactivity	.15	.177
			HF-HRV reactivity	.20	.842	HF-HRV reactivity	.07	.569
						Baseline PEP x HF-HRV	-.17	.118
Model fit, $F(3, 83) = 3.62, p = .016^*$			Model fit, $F(5, 81) = 2.56, p = .034^*$			Model fit, $F(6, 80) = 2.59, p = .024^*$		
$R^2 = .116$			F change (2, 81) = .96, $p = .387$			F change (1, 80) = 2.50, $p = .118$		
			$R^2 = .136$			$R^2 = .16$		

APPENDIX B: SUPPLEMENTAL FIGURE FOR CHAPTER 3

Figure S1. *ERPs at All 32 Electrode Sites Including Ocular Channels for Children.*



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